ENDOTEX™
INTERVENTIONAL SYSTEMS

NexStent® Carotid Stent and Delivery System

INSTRUCTIONS FOR USE

CAUTION: Federal (USA) law restricts this device to sale by or on the order of a physician.

Limited to use by physicians experienced in carotid stenting and who have received appropriate training in the use of the NexStent® Carotid Stent and Delivery System. The NexStent® Carotid Stent Delivery System is indicated for use with the FilterWire EZ ™ Embolic Protection System.

Manufactured by:

EndoTex Interventional Systems, Inc.
10231 Bubb Road
Cupertino, CA 95014 USA

Distributed by:

Boston Scientific Corporation
One Boston Scientific Place
Natick, MA 01760-1537
USA
USA Customer Service 888-272-1001

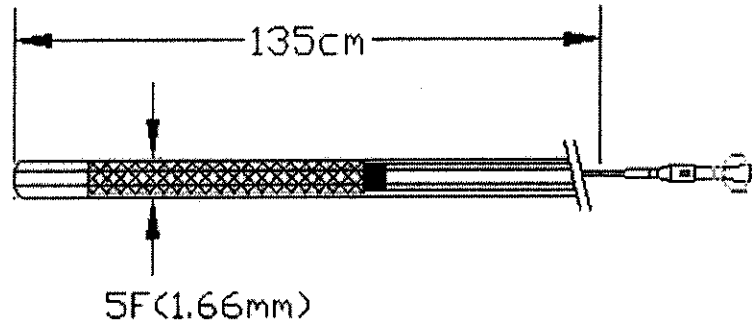
NexStent® Carotid Stent and Delivery System
Information for Prescribers

TABLE OF CONTENTS

1.0 DEVICE DESCRIPTION

The NexStent® Carotid Stent and Delivery System is designed to deliver a self-expanding stent to the extracranial carotid arteries via a sheathed percutaneous delivery system. The NexStent carotid stent is a flexible, self-expanding, rolled Nitinol (nickel-titanium alloy) mesh. One stent size is used for treating vessel diameters ranging from 4mm to 9mm. The length of the stent is 33mm in the delivery system and is approximately 30mm at a fully deployed diameter of 9mm. The stent is constrained within a 5F (1.66mm) Outside Diameter (O.D.) delivery system as shown in Figure 1. Upon deployment into the carotid vasculature, the stent expands to the vessel diameter, imparting an outward radial force on the vessel wall to establish and maintain vessel patency.

Figure 1. The NexStent Carotid Stent and Delivery System



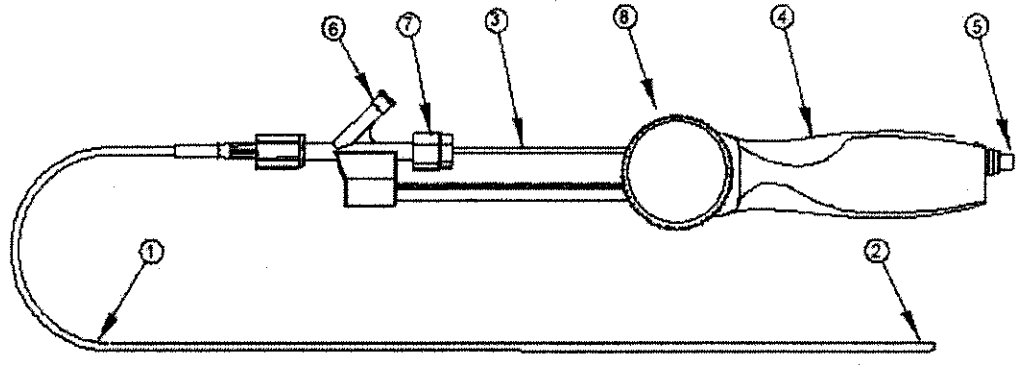
The general features of the NexStent Carotid Stent and Delivery System are shown in Figure 2. The NexStent delivery system is an over-the-wire system (OTW) compatible with standard 0.014in guidewires. The stent is contained within the distal end of a 135cm, 5 French (0.066in O.D.) percutaneous delivery sheath (1). The stent is positioned in the distal end of the delivery system (2) against an inner coil assembly (3) adjacent to a proximal radiopaque marker. The delivery handle (4) controls the relative position of the inner coil assembly, sheath, and stent during stent delivery. The delivery system has two ports: a guidewire port (5) and a Y-connection flush port (6). A luer connector is provided on the guidewire port to enable flushing of the guidewire lumen with heparinized saline prior to use. The delivery sheath and inner coil assembly is flushed via the Y-connection flush port on the Rotating Hemostasis Valve (RHV) (7).

The inner coil assembly extends through the entire sheath and stent. The proximal end of the inner coil assembly is fixed to the delivery handle. Stent positioning is assisted by fluoroscopic visualization of the constrained stent and the radiopaque marker mounted within the inner coil assembly just proximal to the stent. The stent is deployed by rotating the control knob (8) counter-clockwise, thus retracting the sheath. The distal end of the sheath opens as it is withdrawn over the stent and the stent gradually

expands to meet the vessel wall. The stent releases from the delivery system and fully expands against the vessel wall when the sheath is retracted beyond the proximal edge of the stent.

The control knob cannot be rotated to move the sheath forward (i.e. the stent cannot be recaptured). Once the stent has been released into the vessel, the entire delivery system is removed.

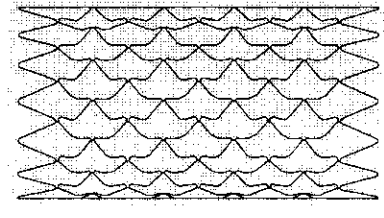
Figure 2. The NexStent® Carotid Stent Delivery System



The NexStent System is available in a single 30mm stent length that accommodates reference vessel diameters between 4mm and 9mm. The NexStent adapts to both straight and tapered vessel anatomies. See Table 1 for recommended reference vessel diameter.

The NexStent System is compatible with either an 8F guiding catheter or a 6F introducer sheath (min. ID 0.087in / 2.21mm). It is also compatible with the FilterWire EZ™ Embolic Protection System..

Table 1. NexStent Carotid Stent



Stent Length (mm)	Reference Vessel Diameter (mm)
30	4.0-9.0

2.0 INDICATIONS FOR USE

The NexStent® System used in conjunction with FilterWire EZ™ Embolic Protection System, is indicated for treatment of patients at high risk for adverse events from carotid endarterectomy (See Section 8 of these instructions) who require carotid revascularization and meet the criteria outlined below:

1. Patients with neurological symptoms associated with ≥50% stenosis of the common or internal carotid artery OR patients without neurological symptoms and ≥80% stenosis of the common or internal carotid artery by ultrasound or angiogram **AND**
2. Patients must have a reference vessel diameter within the range of 4mm and 9mm at the target lesion and a stenosis less than 30mm in length.

3.0 CONTRAINDICATIONS

The NexStent System is contraindicated for use in:

- Patients in whom anticoagulant and/or antiplatelet therapy is contraindicated.
- Patients with severe vascular tortuosity or anatomy that would preclude the safe introduction of the Guiding Catheter/ Sheath, , Embolic Protection System, Delivery Catheter, and/or Retrieval Catheter.
- Patients with a known hypersensitivity to nickel-titanium.
- Patients with uncorrected bleeding disorders.
- Lesions in the ostium of the common carotid artery.

4.0 WARNINGS

WARNING: Only physicians who have received appropriate training and are familiar with the principles, clinical applications, complications, side effects and hazards commonly associated with carotid interventional procedures should use this device.

General

Refer to the Instructions for Use supplied with any interventional device to be used in conjunction with the NexStent System for intended uses, contraindications, and potential complications.

The safety and efficacy of the NexStent® Carotid Stent and Delivery System has not been demonstrated with embolic protection systems other than the FilterWire EZ Embolic Protection System.

The long-term performance (>1 year) of the NexStent® Carotid Stent has not been established.

As with any type of vascular implant, infection secondary to contamination of the stent may lead to thrombosis, pseudoaneurysm, or rupture.

Stenting across a major bifurcation may limit access for future diagnostic or therapeutic procedures.

In patients requiring the use of antacids and / or H2-antagonists before or immediately after stent placement, oral absorption of antiplatelet agents (e.g. aspirin) may be adversely affected.

Only physicians who have received appropriate training and are familiar with the principles, clinical applications, complications, side effects and hazards commonly associated with carotid stent placement should use this device.

Appropriate antiplatelet and anticoagulation therapy should be administered pre- and post-procedure as suggested in these instructions. Special consideration should be given to those patients with recently active gastritis or peptic ulcer disease or other bleeding disorders.

When multiple stents are required, stent materials should be of similar composition.

The Safety and Effectiveness of the NexStent Carotid Stent System has NOT been established in patients with the characteristics noted below.

- Treatment of carotid lesions in patients with carotid artery disease who are not at high risk for carotid endarterectomy.
- Previously placed stent in target artery.
- Total occlusion of the target lesion.
- Angiographic visible thrombus.
- Carotid string sign (a tiny, long segment of contrast in the true lumen of the artery).
- Vessel anatomy precluding the use of the stent system or appropriate positioning of the embolic protection system.
- Presence of carotid artery dissection prior to initiation of the procedure.
- Evidence of a stroke within the previous 30 days.
- History of ipsilateral stroke with fluctuating neurologic symptoms within 1 year.
- History of intracranial hemorrhage within the past 3 months.
- Any condition that precluded proper angiographic assessment or made percutaneous arterial access unsafe, (e.g. morbid obesity, sustained systolic blood pressure >180 mmHg).
- Contraindication to aspirin, or to clopidogrel AND ticlopidine, or stent material.
- History or current indication of bleeding diathesis or coagulopathy including thrombocytopenia or an inability to receive heparin in amounts sufficient to maintain an activated clot time at >250 seconds.
- Hemoglobin (Hgb) <8gm/dl (unless on dialysis), platelet count < 50,000, INR > 1.5 (irreversible), or heparin-associated thrombocytopenia.
- Known cardiac sources of emboli.
- Atherosclerotic disease involving adjoining vessels precluding safe placement of the guiding catheter or sheath.
- Other abnormal angiographic findings that indicated the patient was at risk of a stroke due to a problem other than that of the target lesion, such as: ipsilateral arterial stenosis greater in severity than the target lesion, cerebral aneurysm, or arteriovenous malformation of the cerebral vasculature.
- Severe dementia.
- Life threatening allergy to contrast media that could not be treated.
- Pregnant patients or patients under the age of 18.
- Patients in whom femoral access is not possible.
- Patients with aneurysmal dilation immediately proximal or distal to the lesion.

The safety and effectiveness of concurrent treatment of lesions in patients with bilateral carotid artery disease have not been established

Device Use

- This device is intended for single-use only. **DO NOT** reuse. **DO NOT** resterilize, as this can compromise device performance and increase the risk of cross contamination due to inappropriate reprocessing.
- Do not use the product after the "Use By" date specified on the package.
- Do not use the product if temperature exposure has exceeded 60°C or if the indicator on the box has turned from light gray to black.
- Maintain the patient's Activated Clotting Time (ACT) at >275 seconds throughout the NexStent® System and distal protection usage to prevent thrombus formation on the devices.
- Maintain continuous flush while removing and reinserting devices on the guidewire. Perform all exchanges slowly to prevent air embolism or trauma to the artery.
- Implanting a stent may lead to dissection of the vessel distal and/or proximal to the stent and may cause acute closure of the vessel, requiring additional intervention (carotid endarterectomy, further dilatation, or placement of additional stents).
- The stent may cause a thrombus, distal embolization or may migrate from the site of implant down the arterial lumen. Appropriate sizing of the stent to the vessel is required to reduce the possibility of stent migration. In the event of thrombosis of the expanded stent, thrombolysis and PTA should be attempted.
- In the event of complications such as infection, pseudoaneurysm or fistulization, surgical removal of the stent may be required.
- Overstretching of the artery may result in rupture and life-threatening bleeding.
- If a filter-based embolic protection system is used, allow for and maintain adequate distance between the filter and the stent delivery system or deployed stent to avoid potential entanglement.
- Ensure optimal positioning of the stent prior to deployment. Once deployment is initiated, the stent cannot be repositioned or recaptured. Stent retrieval methods (use of additional wires, snares and/or forceps) may result in additional trauma to the carotid vasculature and/or the vascular access site. Complications may include death, stroke, bleeding, hematoma or pseudoaneurysm.

5.0 PRECAUTIONS

5.1 Stent Handling – Precautions

Carefully inspect the NexStent® System to verify that the device has not been damaged in shipment.

Do not use damaged equipment. Take care to avoid unnecessary handling, which may kink or damage the delivery system.

Do not use if device is kinked.

Do not use if the stent is partially deployed.

Do not expose the delivery system to organic solvents (e.g. alcohol) as structural integrity and/or function of the device may be impaired.

Do not remove the stent from its delivery system as removal may damage the stent. The stent and the delivery system are intended to perform as a system. If removed, the stent cannot be put back in the delivery system.

Precautions to prevent or reduce clotting should be taken when any interventional device is used. Flush or rinse all devices entering the vascular system with sterile isotonic heparinized saline prior to use.

The delivery system should not be used in conjunction with other stents. Special care must be taken not to handle or in any way disrupt the stent in the delivery system.

5.2 Stent Placement - Precautions

Use with bleed-back control hemostatic valves is not recommended.

The NexStent® System is not compatible with any guidewire larger than 0.014in (0.36mm).

The NexStent System must be used with a guiding catheter or introducer sheath to maintain adequate support of the 0.014in guidewire throughout the procedure.

Do not attempt to reposition the Delivery System once the stent has made contact with the vessel wall.

Ensure the stent system is fully flushed with heparinized saline prior to use. Do not use the delivery system if flush is not observed exiting at the distal end of the sheath.

Do not attempt to pull a partially expanded stent back through the guiding catheter or sheath; dislodgment of the stent from the delivery system may occur.

Venous access should be available during carotid stenting to manage bradycardia and/or hypotension by either pharmaceutical intervention or placement of a temporary pacemaker, if needed.

When catheters are in the body, they should be manipulated only under fluoroscopy. Radiographic equipment that provides high quality imaging is needed.

The delivery system is not designed for use with power injection. Use of power injection may adversely affect device performance.

If resistance is met during delivery system introduction, the system should be withdrawn and another system used.

Prior to stent deployment, remove all slack from the delivery system.

5.3 Post-Implant – Precautions

Care must be exercised when crossing a newly deployed stent with other interventional devices to avoid disrupting the stent geometry and placement of the stent. In the event of thrombosis of the expanded stent, thrombolysis and PTA should be attempted.

If more than one stent is required to cover the lesion or if there are multiple lesions, the distal lesion would be stented first, followed by stenting of the proximal lesion.

If overlap of sequential stents is necessary, the amount of overlap should be kept to a minimum. An overlap of 5mm is generally considered acceptable.

5.3.1 Length of Follow up / Special Patient Populations

The safety and efficacy of the NexStent® Carotid Stent beyond 12 months of follow up has not been established in patients that are at high risk for carotid endarterectomy.

5.3.2 Magnetic Resonance Imaging (MRI) Compatibility

- Non-clinical testing of the NexStent Carotid Stent has shown it to be MRI safe at field strengths of 3.0 Tesla or less and a whole body averaged specific absorption rate (SAR) of 2.0 W/kg and special peak SAR of 4.0 W/kg at a maximum MRI exposure of 15 minutes. This level of exposure to radiofrequency (RF) exceeds that typically used for clinical MRI procedures.
- Non-clinical testing has shown that, with a stent orientation of 45 degrees to the angle of the MRI field, stent migration is unlikely to occur in environments of 3.0 Tesla.
- Non-clinical testing has been performed to ensure the stent produced a temperature rise of less than or equal to 0.2°C. The imaging parameters produced an MRI system reported value for the whole body averaged SAR of 2.0 W/kg and special peak SAR of 4.0 W/kg at a maximum MRI exposure of 15 minutes.
- The effect of heating in the MRI environment for overlapping stents or stents with fractured struts is not known.
- MRI quality may be compromised if the area of interest is in the exact same area as or relatively close to the position of the stent.

6.0 ADVERSE EVENTS

6.1 Observed Adverse Events

In the CABERNET trial, the NexStent Carotid Stent and Delivery System (OTW) was evaluated for the treatment of patients with significant extracranial carotid artery stenosis who required carotid revascularization and were at high risk for adverse events from carotid endarterectomy. A total of 454 patients were enrolled in the main registry of the trial.

The primary endpoints of the trial were:

1. Major clinical events at one-year defined as any death, stroke or myocardial infarction (MI).

2. Thirty-day event rate defined as any death, stroke or MI ≤30 days post-procedure; plus the 31-day to 12-month event rate defined as any ipsilateral stroke including any death as a result of an ipsilateral stroke.

The primary objective of the trial was to demonstrate that the major adverse event (MAE) rates for both primary endpoints were not inferior to an Objective Performance Criteria (OPC) derived from the MAE rate historically associated with carotid endarterectomy (CEA).

Tables 2 and 3 present the MAE and the serious adverse events (SAE) reported for the enrolled patients through 1 year. Table 4 presents the patient deaths by causation. The major adverse events table summarizes all deaths, strokes and MIs.

TABLE 2. Major Adverse Events

Major Adverse Events	≤30 days (n=438) [1]		31-365 days (n=421) [2]		Cumulative 0-365 Days (n=421) [2]	
Primary Endpoints	# Patients	%	# Patients	%	# Patients	%
All Death Stroke and MI at 1 Yr.	17	3.9	33	7.8	50	11.9 [4]UCL=14.8 %
	# Patients	%Patients (N=438)	# Patients	% Patients (N=404)[3]	# Patients	% Patients (N=404)[3]
All Death Stroke and MI ≤ 30 days; plus the 31-day to12-month event rate defined as any ipsilateral stroke including any death as a result of an ipsilateral stroke	17	3.9	3	0.7	19	4.7 UCL=6.8%
Major Adverse Events by Classification	≤30 days (n = 438)		31-365 days (n = 421) [2]		Cumulative 0-365 Days (n = 421) [2]	
	# Patients	%	# Patients	%	# Patients	%
Death	2	0.5	17	4.0	19	4.5
Stroke	15	3.4	8	1.9	21	5.0
Ipsilateral Stroke	12	2.7	3	0.7	14	3.3
Major	5	1.1	1	0.2	5	1.2
Minor	7	1.6	2	0.5	9	2.1
Non-Ipsilateral Stroke	3	0.7	6	1.4	8	1.9
Major	1	0.2	3	0.7	4	1.0
Minor	2	0.5	3	0.7	4	1.0
Myocardial Infarction (MI)	1	0.2	16	3.8	17	4.0

[1] N= Patients enrolled in main trial registry (N=454) less patients not stented (N= 11), patients lost to follow-up at 30-day evaluation period (N=3) and patients who had a missed visit at the 30-day timepoint (N=2)

[2] N=421 for the 31-365 and 0-365 time periods. This includes 398 patients evaluated at 1 year, 19 deaths, and 4 patients that did not have a 1-year visit but experienced an adverse event (398+19+4 = 421).

[3] In an effort to present the most conservative analysis for the MAE rate concerning the composite Primary Endpoint N=404 was used. Seventeen patient deaths that occurred during the 31-365 day time period were not due to ipsilateral stroke and were excluded from this analysis. Therefore N = 404 (421-17=404).

[4] Upper Confidence Limit

TABLE 3. Serious Adverse Events

Event Categories[1]	≤ 30 days (N = 454)		31-365 days (N =443)		0-365 Days (N =454)	
	# Patients	% Patients	# Patients	% Patients	# Patients	% Patients
Procedure Related						
Angina	3	0.7	0	0.0	3	0.7
Bleeding/Anemia[2]	16	3.5	1	0.0	17	3.7
Cardiac Dysrrhythmia	14	3.1	0	0.0	14	3.1
Cardiogenic Shock	1	0.2	0	0.0	1	0.2
Ischemia/ ↑ Enzymes	4	0.9	0	0.0	4	0.9
Syncope	4	0.9	0	0.0	4	0.9
Cerebrovascular	3	0.7	0	0.0	3	0.7
Emergent CEA	1	0.2	0	0.0	1	0.2
Genitourinary	1	0.2	0	0.0	1	0.2
Hypotension	19	4.2	0	0.0	19	4.2
Hypertension	1	0.2	0	0.0	1	0.2
Infection	3	0.7	0	0.0	3	0.7
Metabolic	5	1.1	0	0.0	5	1.1
Musculoskeletal	2	0.4	0	0.0	2	0.4
Neurological	11	2.4	0	0.0	11	2.4
Prolonged Hospitalization	1	0.2	0	0.0	1	0.2
Respiratory	2	0.4	0	0.0	2	0.4
Vascular	7	1.5	5	1.1	12	2.6
Other	2	0.4	0	0.0	2	0.4
Access Site Complications[3]						
Bleeding and Hematoma	9	2.0	0	0.0	9	2.0
Ecchymosis	1	0.2	0	0.0	1	0.2
Pseudoaneurysm	3	0.7	1	0.2	4	0.9
Poss. Femoral Artery Thrombosis	1	0.2	0	0.0	1	0.2
Wound Infection	2	0.4	0	0.0	2	0.4
Total Procedure related	80	17.6	7	1.6	85	18.7
Non-Procedure Related						
Cardiac						
Angina	2	0.4	20	4.5	22	4.8
Cardiogenic Shock	0	0.0	1	0.2	1	0.2
Congestive Heart Failure (CHF)	3	0.7	16	3.6	19	4.2
Coronary Artery Disease	2	0.4	26	5.9	28	6.2
Dysrrhythmia	2	0.4	12	2.7	14	3.1
Ischemia/ ↑ Enzymes	3	0.7	3	0.7	5	1.1
Syncope	1	0.2	1	0.2	1	0.2
Valvular Disease	0	0.0	5	1.1	5	1.1
Other	1	0.2	2	1.1	3	0.7
Neurological						
TIA	0	0.0	8	1.8	8	1.8
Altered Mental Status	1	0.2	2	0.5	3	0.7
Organic Brain	0	0.0	2	0.5	2	0.4

Event Categories[1]	≤ 30 days (N = 454)		31-365 days (N =443)		0-365 Days (N =454)	
	# Patients	% Patients	# Patients	% Patients	# Patients	% Patients
Syndrome/Memory Loss						
Seizure	1	0.2	2	0.5	3	0.7
Syncope/Dizziness	1	0.2	11	2.5	12	2.6
Visual Disturbance	0	0.0	2	0.5	2	0.4
Other	0	0.0	1	0.2	1	0.2
Other Systems						
Bleeding	2	0.4	8	1.8	10	2.2
Blood Dyscrasia	9	2.0	9	2.0	17	3.7
Carcinoma	1	0.2	9	2.0	10	2.2
Cerebrovascular	0	0.0	5	1.1	5	1.1
Gastrointestinal	6	1.3	30	6.8	35	7.7
Genitourinary	3	0.7	1	0.2	4	0.9
Hemodynamic	2	0.4	7	1.6	9	2.0
Infection	2	0.4	10	2.3	12	2.6
Metabolic	2	0.4	10	2.3	12	2.6
Musculoskeletal	1	0.2	13	2.9	14	3.1
Other Hospitalization	0	0.0	22	5.0	22	4.8
Respiratory	2	0.4	18	4.1	19	4.2
Vascular[4]	4	0.9	42	9.5	45	9.9
Other	6	1.3	7	1.6	11	2.4
Total Non-Procedure Related	46	10.1	186	42.0	206	45.4

[1] Patients may have had multiple events and therefore can be counted in more than one category/subcategory of event. Counts represent the number of patients who have experienced one or more events.
[2] Twenty patients that had procedure related bleeding (non-access site) required a blood transfusion; 14 of the 20 events were procedure related
[3] Six access site complications required blood transfusions.
[4] Three of the 9 patients reported as having restenosis are not included in the "Vascular" event category secondary to AE forms which were pending for "target lesion restenosis"; however the 3 patients are reported in the secondary endpoint for restenosis.

Events are categorized by body system and are defined as follows:

- Access site includes such events as aneurysm, bleeding, bruising or ecchymosis, hematoma, pseudo-aneurysm, pain and arterial thrombosis.
- Bleeding includes such non access-site bleeding, nose bleed, surgical or incisional bleeding and retroperitoneal bleed.
- Blood Dyscrasia includes events such as anemia, thrombocytopenia, and leucopenia.
- Carcinoma includes such events as lung cancer, breast cancer, leukemia, brain tumor, rectal cancer.
- Cardiac includes such events as angina, coronary artery disease, cardiac dysrrhythmia, congestive heart failure cardiac-related syncope and valvular disease (aortic and mitral).
- Cerebrovascular includes such events as headache and brain hemorrhage.
- Gastrointestinal includes events such as dysphagia, indigestion, nausea, vomiting, esophageal stenosis or varicies, ulcer, bowel obstruction, GI Bleed, colitis, cholecystitis, pancreatitis, hepatic disorders, diverticulitis, melena and rectal prolapse.

- Genitourinary includes events such as urinary retention, hematuria, nocturia related to prostatic hyperplasia and lower abdominal pain related to the bladder or prostate.
- Hemodynamic includes events such as hypotension and hypertension
- Metabolic includes events such as diabetes, dehydration, electrolyte imbalance and renal failure.
- Musculoskeletal includes events such as bone, muscle or joint pain, fractures and arthritis injury, and inguinal hernia.
- Infection includes events such as conjunctivitis, cellulitis, parotitis, abscess, system infection, sepsis, fungal infection, urinary tract infection, wound infection and non-specified infection.
- Neurological includes all non-stroke related events such as altered mental status/confusion/dementia/organic brain syndrome, seizure, sensory deficits (peripheral numbness or weakness), visual/speech disturbances, neurologic-related syncope or dizziness, and TIA.
- Respiratory includes events such as pneumonia, hemoptysis, respiratory. failure and chronic obstructive lung disease.
- Vascular includes such as events as carotid restenosis (target and non-target lesion), peripheral arterial disease, and peripheral arterial or venous thrombosis.
- Other Hospitalizations include hospitalizations for other medical/surgical treatment.
- Other is a miscellaneous category that includes such events as agitation, drug hypersensitivity, patient fall (non-neurologic) rash, general weakness, gout, peripheral edema, fatigue etc.

TABLE 4. Patient Deaths

Event Categories	Total (n=421)	
	Deaths	%
0-30 days		
Cardiac	1	0.2
Sepsis	1	0.2
31-365 days		
Cardiac	9	2.1
Carcinoma	2	0.5
Respiratory	2	0.5
Gastrointestinal	1	0.2
Renal Failure	1	0.2
Liver Failure	1	0.2
Unknown	1	0.2
Total Deaths (0-365 days)	19	4.5

Note: There were no neurologic related deaths

6.2 Potential Adverse Events

Based on the literature and on clinical and commercial experience with carotid stents and embolic protection systems, the following alphabetical list includes possible adverse events associated with use of these devices:

- Allergic reactions to anti-platelet agents/contrast medium
- Aneurysm
- Angina/coronary ischemia
- Arrhythmia
- Arterial occlusion/thrombosis at puncture site or remote site
- Arteriovenous fistula
- Bacteremia or septicemia
- Bleeding from anticoagulant or antiplatelet medications
- Cerebral edema
- Cerebral hemorrhage
- Cerebral ischemia/transient ischemia attack (TIA)
- Congestive heart failure (CHF)
- Death
- Detachment and/or implantation of a component of the system
- Emboli, distal (air, tissue or thrombotic emboli)
- Emergent or urgent endarterectomy surgery (CEA)
- Fever
- Filter thrombosis/occlusion
- Groin hematoma, with or without surgical repair
- Hemorrhage, with or without transfusion
- Hyperperfusion syndrome
- Hypotension/hypertension
- Infection and pain at insertion site
- Ischemia/infarction of tissue/organ
- Myocardial infarction (MI)
- Pain (head, neck)
- Pseudoaneurysm, femoral
- Renal failure/insufficiency
- Restenosis of stented segment
- Seizure
- Severe unilateral headache
- Stent/filter entanglement/damage
- Stent embolization
- Stent malposition
- Stent migration
- Stent thrombosis/occlusion
- Stroke/cerebrovascular accident (CVA)
- Total occlusion of carotid artery
- Vessel dissection, perforation, or rupture
- Vessel spasm or recoil

Any device related adverse event occurring involving the NexStent® Carotid Stent System should be reported immediately to Boston Scientific Corporation at (888) 272-1001.

7.0 CABERNET Trial

The Carotid Artery Revascularization Using the Boston Scientific EPI FilterWire EX/EZ system and the EndoTex NexStent (CABERNET Trial) was a prospective, non-randomized multicenter clinical trial evaluating the safety and efficacy of the NexStent Carotid Stent and Delivery System (NexStent) in conjunction with the Boston Scientific FilterWire EX System and EZ System. The CABERNET study protocol included implantation of the NexStent for the treatment of patients with significant extracranial carotid artery stenosis who required carotid revascularization and were at high risk for adverse events from carotid endarterectomy. An overview of the clinical trial is provided in Table 5. High risk for carotid endarterectomy was established with anatomical and co-mordid conditions. The study was designed to demonstrate an adverse event rate not greater than the historical control (12.1%) plus an additional delta of 4% established for this study (16.1%).

Table 5. CABERNET Trial Overview

Title:	Carotid Artery Revascularization Using the Boston Scientific FilterWire EX/EZ System and the EndoTex NexStent.
Products Evaluated	EndoTex NexStent in conjunction with Boston Scientific FilterWire EX System or EZ System.
Study Design:	A prospective, non-randomized, multicenter clinical trial.
Clinical Sites:	A total of 21 Sites participated in the trial. At two sites the study was transitioned to other institutions. Of the remaining 19 sites, there were 15 US sites and 4 OUS sites.
Primary Endpoints[6]:	**Safety** 1) Major clinical events at one-year defined as any death, stroke or myocardial infarction 2) 30-day event rate defined as any death, stroke or MI ≤ 30-days post-procedure; plus the 31-day to12-month event rate defined as any ipsilateral stroke including any death as a result of an ipsilateral stroke.
Secondary Endpoints:	**Safety and Efficacy** NexStent Technical Success[1] FilterWire Technical Success[1] Overall System Technical Success[1] Angiographic Success[2] Procedure Success[3] Restenosis [4] Target Vessel Revascularization[5]
Study Hypothesis	Non-Inferiority compared to a historical control for patients at high risk for CEA.
Patient Follow-up	Follow-up Visits: Hospital Discharge, 1-Month, 6-Month, 12-Month, 2-Year, 3-Year.

[1]Technical Success rates were based on the devices being placed and retrieved as described in the study protocol.
[2]Angiographic Success was achievement of ≤50% residual stenosis based on the original diameter of the target lesion.
[3]Procedural Success was defined as patients who had angiographic success, overall system success and MAE free within 24 hours of the index procedure.
[4]Restenosis was defined >80% narrowing of the target lesion based on the Strandness criteria that occurred >1 month post procedure.
[5]Target Vessel Revascularization was defined as any narrowing of the target lesion or vessel >1 month post procedure, requiring revascularization.
[6]The primary endpoints of the trial were evaluated at 1 year.

The primary endpoints of the trial were:

1. Major clinical events at one-year defined as any death, stroke or myocardial infarction (MI).

2. Thirty day event rate defined as any death, stroke or MI ≤30-days post-procedure; plus the 31-day to12-month event rate defined as any ipsilateral stroke including any death as a result of an ipsilateral stroke.

The primary objective of the trial was to demonstrate that the major adverse event (MAE) rates for both primary endpoints were not greater than the MAE events rates associated with high-risk carotid endarterectomy (12.1%) plus an additional delta of 4% established for this study (16.1%).

The study hypotheses were compared to a historical control for adverse events occurring in high-risk patients undergoing carotid endarterectomy (11% for anatomical risk factor and 14% for comorbidity), plus a statistical equivalence delta of 4 percentage points. The weighting factors for the adjusted adverse event rate (OPC) were determined by the observed case mix of anatomical high-risk patients vs. co-morbid high-risk patients in this patient sample.

The null hypothesis of study device system inferiority to control was tested against the alternative hypothesis of equivalence (non-inferiority) to control.

H_0: $P \geq OPC + 0.04$
H_a: $P < OPC + 0.04$

The hypotheses were tested by calculating a normal approximation to the binomial test statistic, Z. If $Z > Z_{0.05} = 1.645$ (the weighted OPC plus equivalence threshold) then the null hypothesis of inferiority will be rejected and the study device system was considered equivalent to CEA.

Patients were followed at hospital discharge, 1-Month, 6-Months, and 1-Year. Additionally, registry patients will be followed annually through 3 years from the date of the index procedure. Patients were seen in follow-up by the treating physician as well as independent neurologist (neurological assessments). Core laboratories were utilized for the analysis of angiographic, ultrasound, ECG and CT/MRI (only for evaluation of neurological events or symptomology) data. To ensure patient safety, medical monitors reviewed safety data to ensure appropriate reporting of adverse events.

A Clinical Events Committee (CEC) reviewed all reported major adverse events for the primary endpoint and a Data Safety Monitoring Board (DSMB) reviewed the summary of these events to ensure patient safety.

Eligibility Criteria Summary

The study population consisted of male and female patients, at least 18 years of age, with discrete lesions in the internal or common carotid artery or the carotid bifurcation. Patients had to be high-risk candidates for carotid endarterectomy (CEA); both symptomatic (≥50% stenosis) and asymptomatic (≥60% stenosis by angiography, 80% stenosis by ultrasound) patients were eligible.

Inclusion Criteria

Key inclusion criteria included the following:

- Lesion is located in the common carotid artery (CCA) and/or the internal carotid artery (ICA) or the carotid bifurcation.
- Target vessel is the only vessel being treated at this intervention and the lesion is ≤30mm and can be treated with a single stent.
- Vessel to be treated is between 4mm and 9mm in diameter.
- Distal vessel "landing zone" for placement of the FilterWire must be between 3.5 mm and 5.5mm in diameter and have available the following artery lengths:
  - A minimum of 2.0cm distal to the target lesion.
  - A minimum of 2.0cm straight vessel segment for placement of the filter.
  - A minimum of 1.0cm from a major vessel curve.

Patients were required to meet one of the following criteria:

- **Symptomatic:** Stenosis must be ≥50% as determined by duplex ultrasound and angiogram; and the patient has a history of stroke, TIA and/or amaurosis fugax in the hemisphere supplied by the target vessel within 180 days of the procedure.

OR

- **Asymptomatic:** Stenosis must be ≥80% as determined by duplex ultrasound and ≥60% as determined by angiogram without any neurological symptoms.

Eligible patients were required to meet at least one of the following high risk anatomical conditions, one of the Class I high risk comorbid conditions or two of the Class II high risk comorbid conditions criteria in order to be eligible to participate in the study:

Anatomical High-Risk Conditions

1. Previous carotid endarterectomy with significant restenosis (as defined above for symptomatic or asymptomatic patients).
2. Total occlusion of the contralateral carotid artery.
3. Previous radiation treatment to the neck or radical neck dissection.
4. Target lesion is at or above the second vertebral body (C2) or below the clavicle.
5. Inability to extend the head due to cervical arthritis or other cervical disorders.
6. Tracheostomy or tracheal stoma.
7. Presence of laryngeal nerve palsy.
8. Bilateral carotid artery stenosis as determined by angiography in which both carotid arteries require treatment, as defined as:
   a. Bilateral asymptomatic stenosis ≥60% or,
   b. Bilateral symptomatic stenosis ≥50% or,
   c. Bilateral stenoses, one side with a symptomatic stenosis ≥50% and the other side asymptomatic with a stenosis ≥60%.

Comorbid High-Risk Conditions

CLASS I HIGH RISK (Only one of the following were required)

1. Unstable angina (rest pain with ECG changes).

2. Known severe left ventricular dysfunction, (LVEF) <30%.
3. Congestive heart failure (CHF) - New York Heart Association Functional Class III or IV.
4. Dialysis dependent renal failure.
5. Chronic obstructive pulmonary disease (COPD) with either: Forced Expiratory Volume in 1 Second (FEV1) <50% predicted or, Chronic oxygen therapy or, Resting PO2 of ≤60 mmHg or, baseline hematocrit ≥50%.
6. Requirement for staged CABG or valve replacement post carotid index procedure.

CLASS II HIGH RISK (Two of the following were required)

1. Patient is ≥75 years of age.
2. Myocardial infarction within previous 6 weeks.
3. Requires staged peripheral vascular surgery (i.e. abdominal aortic aneurysm repair) or other major surgery post carotid index procedure.
4. Two or more proximal or major diseased coronary arteries with ≥70% stenosis that have not or cannot be revascularized.

Exclusion Criteria

A patient with any of the following criteria was not considered eligible for treatment in the trial.

1. Previously placed stent in target vessel.
2. Total occlusion of target vessel (ICA or CCA).
3. Angiographically visible thrombus.
4. Carotid string sign (a tiny, long segment of contrast in the true lumen of the artery, aneurysmal pouch formation, and the distal location of the arteriopathy) with poor visualization of the distal vessel.
5. Vertebrobasilar insufficiency symptoms only, without clearly identifiable symptoms referable to the targeted carotid artery.
6. Vessel anatomy precluding use of stent system or distal protection system.
7. Presence of carotid artery dissection.
8. Requirement for staged CABG, valve replacement or abdominal aortic aneurysm procedure ±30 days of the index procedure.
9. Evidence of a major disabling stroke within the previous 30 days.
10. Patient has an evolving stroke or has experienced a major stroke (NIHSS score ≥15) within 3 months.
11. History of intracranial hemorrhage within the past 12 months.
12. Any condition that precludes proper angiographic assessment or makes percutaneous arterial access unsafe, e.g. morbid obesity, history of chronic hypertension that is not controlled by medical therapy.
13. Contraindication to heparin, aspirin, clopidogrel (Plavix®), X-ray contrast or ticlopidine (Ticlid®) in cases of intolerance to clopidogrel.
14. History of liver failure with elevated prothrombin time.
15. History or current indication of bleeding diathesis or coagulopathy.
16. Hgb <8gm/dl (unless on dialysis), platelet count <50,000, WBC >15,000, INR >1.5 (irreversible) or heparin-associated thrombocytopenia.

17. Known cardiac sources of emboli not under treatment with anticoagulant therapy.
18. Atherosclerotic disease involving adjoining vessels precluding safe placement of the guiding catheter or sheath.
19. Planned treatment of non-target lesion within 30 days.
20. Other abnormal angiographic findings that indicate the patient is at risk of a stroke due to a problem other that the target lesion, such as: ipsilateral arterial stenosis greater in severity than the target lesion, cerebral aneurysm, or arteriovenous malformation (AVM) of the cerebral vasculature.
21. Dementia or confusion.
22. The patient is enrolled in another study protocol.
23. Patient may not participate in another investigational trial up to 12 months post-index procedure.

Study Population

The first patient was enrolled on February 20, 2002. Enrollment was completed on March 10, 2004. A total of 488 patients enrolled in the CABERNET trial at 21 participating centers worldwide and 41 of the 488 patients also underwent a contralateral procedure (>30 days following initial index procedure). Thirty-four of the 488 patients were enrolled with "Roll-In" status at 16 centers, yielding a total of 454 (488-34) patients enrolled in the main registry of the trial. Eleven patients did not receive a NexStent at the time of implant and were terminated from the study per protocol, yielding a total of 443 evaluable patients at the time of discharge. Three patients were lost to follow-up (LTF) and 2 patients expired after hospital discharge, with 438 patients available for their 1-month follow-up. There were 2 missed visits yielding 436 patients that completed a 1-month follow-up visit. There were 17 patients that were LTF and 17 patients that expired between the 30-day and 1 year follow-up visits, with 404 patients that were available for their 1-year follow-up. There were 6 missed visits at 1 year yielding 398 patients whom completed their 1-year follow-up.

The data analyses for the purpose of the primary endpoints included follow-up through one year as pre-specified in the study. A summary of patient enrollment and disposition is provided in Table 6.

TABLE 6. Patient Enrollment and Disposition

Patient Population	Index Procedure	30-Days	1-Year
Total Number of Patients Enrolled	488		
Roll-In Patients	34		
Patients Enrolled in Main Trial Registry	454		
Patients Without a NexStent Implanted	11		
Evaluable Patients[1]	443	443	443
Patients Lost to Follow-Up or Withdrawals (Cumulative)	0	3	20
Deaths (Cumulative)	0	2	19
Evaluable Patients Available for Follow-up	443	438	404
Total number of planned visits among evaluable patients			
Total Missed Visits among evaluable patients		2	6
Total Patients Evaluated		436	398
Clinical Assessments Performed		428 (97.7%)	377 (93.3%)
Neurologic Assessments Performed		412 (94.1%)	365 (90.3%)
12 Lead ECGs (30-Day FU Only) Performed		335 (76.5%)	
Duplex Ultrasound Exams Performed		387 (88.3%)	331 (81.9%)
Stroke Scales Performed		412 (93.6%)	354 (87.6%)
Total Patient Follow-up Rate		436 (99.5%)	398 (98.5%)

[1] Evaluable patients only include those that have a NexStent implant.

The majority of the patients enrolled in the trial were asymptomatic, Caucasian males with an average age of 72.5 years. Of the 454 patients enrolled in the main registry 63.7% had an anatomical high risk factor, 19.6% had a comorbid high risk factor and 16.7% had both. In terms of baseline lesion characteristics, the majority of the patients had a de novo target lesion located in the internal carotid artery. The mean baseline lesion stenosis was 71.9% with an average length of 13.9mm and average diameter of 1.3mm. Baseline demographics and lesion characteristics for the patient population are provided in Tables 7, 8, and 9. Baseline lesion characteristics were analyzed by a centralized angiographic core laboratory.

TABLE 7. Baseline Demographics

Patient Characteristic		Patients (N = 454)	% (except as noted)
Age (years)	Mean ± SD		72.5 ± 8.6 yrs
	Minimum to Maximum		46 to 94 yrs
Age by Decade of Life	40-49	6	1.3
	50-59	29	6.4
	60-69	124	27.3
	70-79	194	42.7
	80-89	97	21.4
	>90	4	0.9
Gender	Male	297	65.4
	Female	157	34.6
Ethnicity	Caucasian	414	91.2
	African American	21	4.6
	Hispanic	10	2.2
	Asian	5	1.1
	Other	4	0.9
Patient Classification	Symptomatic	110	24.2
	Asymptomatic	344	75.8
Medical History	Diabetes Mellitus	150	33.0
	Liver Failure	0	0.0
	Dyslipidemia	315	69.4
	GI Bleeding/PUD	29	6.4
	Hypertension	377	83.0
	Uncontrolled Hypertension	6	1.3
	Cigarette Smoker	320	70.5
	Current Cigarette Smoker	83	18.3
	Family Hx Premature ASD	74	16.3
	Significant Aortic Arch Atherosclerosis	5	1.1
	Cardiac Arrhythmia	81	17.8
	Valvular Disease	26	5.7
	CAD	283	62.3
	PVD	178	39.2
	Prior PTCA	119	26.2
	Prior Valve Replacement	21	4.6
	Prior CABG	161	35.5
	Prior Carotid PTA	13	2.9
	Prior Carotid Stenting	12	2.6
	Hx of TIA	124	27.3
	Hx of Stroke	96	21.1
	Family Hx of Stroke	52	11.5
	Hx of Seizures	11	2.4
	Hx of Other Neuro	30	6.6
	Prior Vertebrobasilar Intervention	1	0.2
	Other	73	16.1

TABLE 8. Patient High-Risk Inclusion Criteria

Inclusion Criteria	Patients (N=454)	%
High Risk Category		
Anatomical Only	289	63.7
Comorbid Only	89	19.6
Both Anatomic and Comorbid	76	16.7
Class I - Comorbid	139	30.6
Class II - Comorbid	53	11.7
Anatomical High Risk Inclusion Criteria (A)		
Previous CEA	95	20.9
Total Occlusion of Contralateral Carotid Artery	85	18.7
Previous Radial Neck Dissection or Radiation Therapy to Neck Region	30	6.6
Target Lesion at or above C2 or below Clavicle	25	5.5
Spinal Immobility of Neck (cervical arthritis or other)	54	11.9
Tracheostomy or tracheal stoma	3	0.7
Presence of laryngeal nerve palsy	8	1.8
Bilateral Carotid Artery Stenosis	143	31.5
Class I: Comorbid High Risk Inclusion Criteria (CI)		
Unstable Angina	26	5.7
Severe LV Dysfunction	42	9.3
CHF (NYHA Class III/IV)	40	8.8
Renal Failure (Dialysis Dependent)	5	1.1
Severe COPD	38	8.4
Requires Staged CABG or Valve Surgery	21	4.6
Class II: Comorbid High Risk Inclusion Criteria (CII)		
Patient is ≥75 years of Age	199	43.8
MI within 6 weeks	5	1.1
Requires Staged Peripheral Vascular Surgery	34	7.5
Major CAD (≥70 Stenosis that have not or cannot be revascularized)	64	14.1

Table 9. Baseline Lesion Characteristics (Pre-Procedure)

Angiographic Data (Core Laboratory Assessment)		Results	
Parameter		**Patients (N=454)**	**%**
Lesion Type			
de novo		360	79.3
Restenotic		94	20.7
Lesion Morphology[1]			
Eccentric		327	72.0
Ulceration		169	37.2
Calcification		190	41.9
Target Lesion Length (mm)			
Mean ± SD	n=441[2]	13.9 ± 5.9	
Minimum Lumen Diameter (mm)			
Mean ± SD	n=443[2]	1.3 ± 0.6	
Baseline Percent Diameter Stenosis (%)			
Mean ± SD	n=443[2]	71.9 ± 11.0	

[1] Lesions may have had more than one type of morphology
[2] Lesion length was not available in 13 patients; MLD and Percent Diameter Stenosis were not available in 11 patients.

Trial Results

The primary and secondary endpoints evaluating the safety and efficacy of the NexStent® in the CABERNET trial are presented in Table 10 and 11 respectively. The 30-day primary endpoint MAE rate (all death, stroke and MI within 30 days) was 3.9%. The 1-year endpoint MAE rate for all death, stroke and MI was 11.9%. The rate for the composite 1-year endpoint that includes the 30-day MAEs plus ipsilateral stroke or death from ipsilateral stroke within 31-365 days was 4.7%.

The primary endpoints in this study were further explored through a time-to-event analysis using a Kaplan-Meier (KM) estimator for the survival function. Life table estimates were obtained for:

a. Freedom from major adverse events (All Deaths, Strokes and MIs) at 1-Year
b. Freedom from major adverse events (All Deaths, Strokes and MIs) at 30-Days; plus ipsilateral stroke or death related to ipsilateral stroke at 1-Year.

Angiographic success was defined as less than 50% residual stenosis following completion of the stent implantation and was attained in 97.7% (423/433) of evaluable patients. The mean post-procedure residual stenosis was 20.5% as assessed by the core laboratory and 6.45% as per the visual inspection performed by the treating physician at the completion of the procedure. Acute procedure success, defined as the composite of angiographic success and overall technical success without the occurrence of an MAE within 24 hours, was demonstrated in 395 patients (87.0%).

The primary endpoints of the trial were met. The upper confidence limits for both primary endpoint MAE rates (14.8%, 6.8% respectively) fell below the reference OPC (12.1%) plus an additional delta of 4% established for this study (16.1%), allowing acceptance of

the hypothesis that carotid stenting using the NexStent Carotid Stent and Delivery System with the FilterWire EZ™ Embolic Protection System meets acceptance of the study hypothesis of comparability to CAE in the high-surgical-risk study population.

Table 10. Primary Endpoints (Major Adverse Events)

Major Adverse Events	≤30 days (n=438)		31-365 days (n=421) [1]		Cumulative 0-365 Days (n=421) [1]	
Primary Endpoints	# Patients	%	# Patients	%	# Patients	%
All Death Stroke and MI at 1 Yr.	17	3.9	33	7.8	50	11.9 UCL=14.8%
	# Patients	%Patients (N=438)	# Patients	% Patients (N=404) [2]	# Patients	% Patients (N=404) [2]
All Death Stroke and MI ≤ 30 days; plus the 31-day to12-month event rate defined as any ipsilateral stroke including any death as a result of an ipsilateral stroke	17	3.9	3	0.7	19	4.7 UCL=6.8%
Major Adverse Events by Classification	≤30 days (n = 438)		31-365 days (n = 421) [1]		Cumulative 0-365 Days (n = 421) [1]	
	# Patients	%	# Patients	%	# Patients	%
Death	2	0.5	17	4.0	19	4.5
Stroke	15	3.4	8	1.9	21	5.0
Ipsilateral Stroke	12	2.7	3	0.7	14	3.3
Major	5	1.1	1	0.2	5	1.2
Minor	7	1.6	2	0.5	9	2.1
Non-Ipsilateral Stroke	3	0.7	6	1.4	8	1.9
Major	1	0.2	3	0.7	4	1.0
Minor	2	0.5	3	0.7	4	1.0
Myocardial Infarction (MI)	1	0.2	16	3.8	17	4.0

[1] N=421 for the 31-365 and 0-365 time periods. This includes 398 patients evaluated at 1 year, 19 deaths, and 4 patients that did not have a 1-year visit but experienced an adverse event (398+19+4 = 421).

[2] In an effort to present the most conservative analysis for the MAE rate concerning the composite Primary Endpoint N=404 was used. Seventeen patient deaths that occurred during the 31-365 day time period were not due to ipsilateral stroke and were excluded from this analysis. Therefore N = 404 (421-17=404).

Table 11. Secondary Endpoints

Endpoint	Results		95% Confidence Limit (%)
	n/N	%	
FilterWire Technical Success	454/477	95.2	LCL=93.2
NexStent Technical Success	443/470	94.3	LCL=92.2
Overall System Technical Success	422/454	93.0	LCL=90.7
Angiographic Success	423/433	97.7	LCL=96.1
Procedure Success (Acute)	395/454	87.0	LCL=84.1
Restenosis 50-79%			
(Cumulative 0-6 Month)	55/343[1]	16.0%	UCL=19.7
(Cumulative 0-12 Month)	65/347[2]	18.7%	UCL=22.5
Restenosis >80%			
(Cumulative 0-6-Month)	3/340[3]	0.9	UCL=2.3
(Cumulative 0-12-Month)	9/333[4]	2.7	UCL=4.7
Target Vessel Revascularization (6-Month)	4/443	0.9	UCL=2.1
(1-Year)	9/443	2.0	UCL=3.5

[1] N=343 includes all patients with duplex ultrasound data available at 6 months plus any patient without a 6 month evaluation that had 50-79% restenosis at an earlier evaluation (339+4=343).
[2] N=347 includes all patients with duplex ultrasound data available at 12 months, any patient without a 6 month evaluation that had 50-79% restenosis at an earlier evaluation, (331+16=347).
[3] N=340 includes all patients with duplex ultrasound data available at 6 months plus any patient without a 6 month evaluation that had >80% restenosis at an earlier evaluation (339+1=340).
[4] N=333 includes all patients with duplex ultrasound data available at 12 months, any patient without a 12 month evaluation that had >80% restenosis at an earlier evaluation and 1 patient that had a late 1 year follow-up who had >80% restenosis (331+2=333).

Additional Analysis

The primary endpoints in this study were further explored through a time-to-event analysis using a Kaplan-Meier estimator for the survival function. Life table estimates were obtained for:

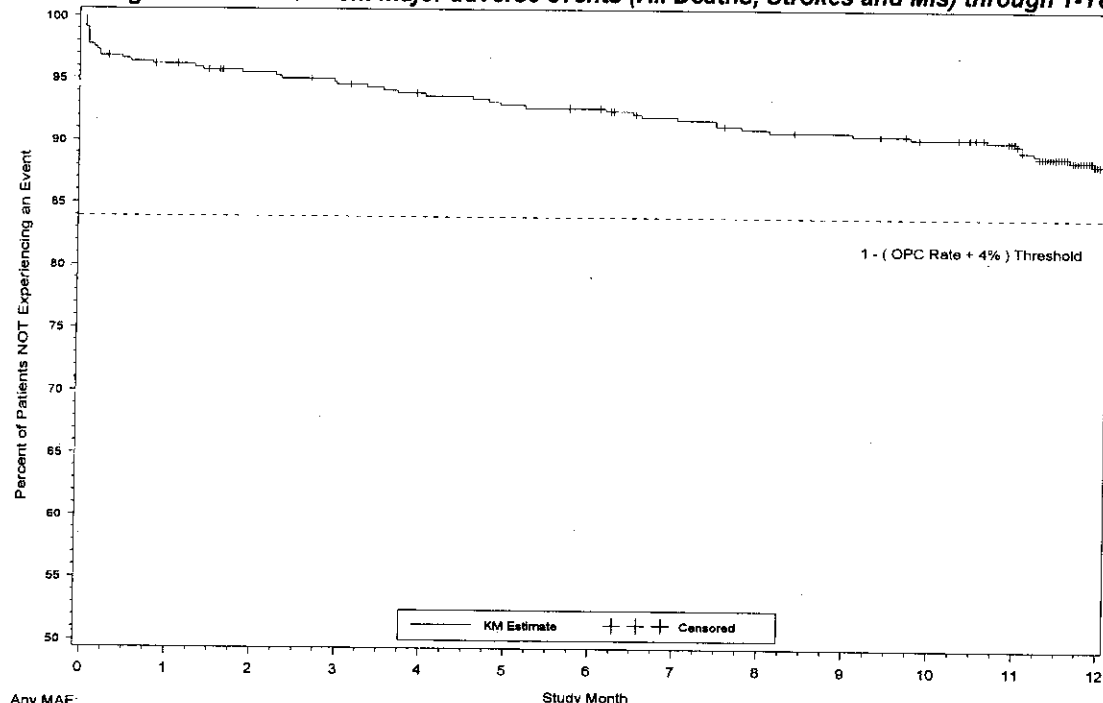
a. Survival from major adverse events (All Deaths, Strokes and MIs) through 1-Year
b. Survival from major adverse events (All Deaths, Strokes and MIs) at 30-Days; plus ipsilateral stroke or death related to ipsilateral stroke through 1-Year.

Endpoint Analysis

Patients were included in these analyses if they had a successful NexStent® implant. The survival time for patients who experienced a major adverse event was calculated as the number of days from the index procedure to the date the adverse event was first identified. For patients who withdrew from the study before the time of analysis, the survival time was calculated as the number of days from the index procedure to the date of their withdrawal. For the composite endpoint, for patients who died of causes unrelated to an ipsilateral stroke, the survival time for the composite endpoint analysis was calculated as the number of days from the index procedure to the date of their death. Patients who were terminated early from the study are considered censored in the analyses performed. Figures 3 and 4 present the KM analysis for each endpoint. Figures 5 through 8 present the KM analysis for asymptomatic and symptomatic patients for each endpoint. The event rate estimate of 11.7% obtained for all death, strokes, and MIs at 12 months from the life table is consistent with the estimate of 11.9% obtained according to the analysis performed per protocol. Similarly, the estimate obtained from

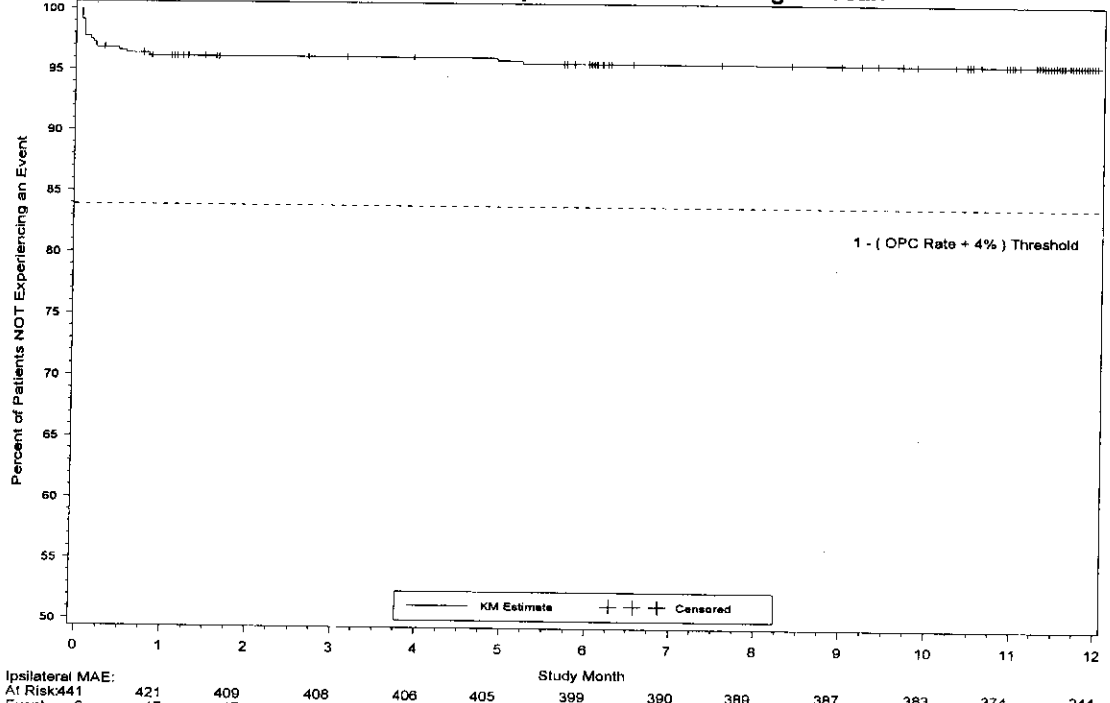
the life table of 4.3% for the event rate for the composite endpoint of major adverse events (All Deaths, Strokes and MIs) at 30-Days; plus ipsilateral stroke or death related to ipsilateral stroke at 1-Year is consistent with the obtained estimate of 4.7% according to the analysis performed per protocol.

Figure 3. ***Survival from major adverse events (All Deaths, Strokes and MIs) through 1-Year***



Any MAE:												
At Risk:	441	422	414	409	404	400	398	389	385	383	378	369	239
Events:	0	17	20	24	27	31	32	36	39	40	42	43	50
Event %:	0.00	3.86	4.54	5.47	6.16	7.09	7.32	8.26	8.97	9.21	9.68	9.93	11.74

Figure 4. Survival from major adverse events (All Deaths, Strokes and MIs) at 30-Days; plus ipsilateral stroke or death related to ipsilateral stroke through 1-Year.



Ipsilateral MAE:												
At Risk:	441	421	409	408	406	405	399	390	389	387	383	374	244
Events:	0	17	17	17	17	18	19	19	19	19	19	19	19
Event %:	0.00	3.86	3.86	3.86	3.86	4.09	4.33	4.33	4.33	4.33	4.33	4.33	4.33

Figure 5: Survival from Major Adverse Events (All Deaths, Strokes and MIs) at One Year
Symptomatic Patient Group

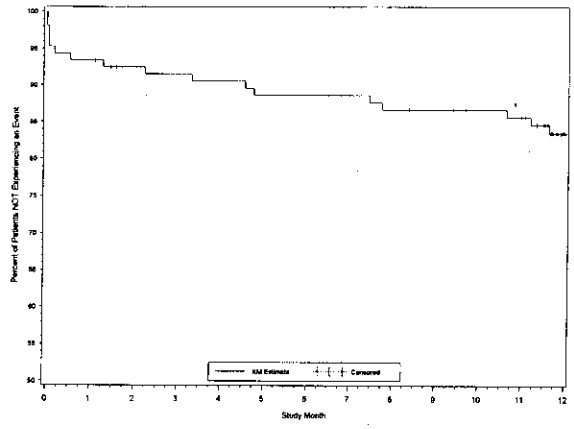


Figure 6: Survival from Major Adverse Events (All Deaths, Strokes and MIs) at One Year
Asymptomatic Patient Group

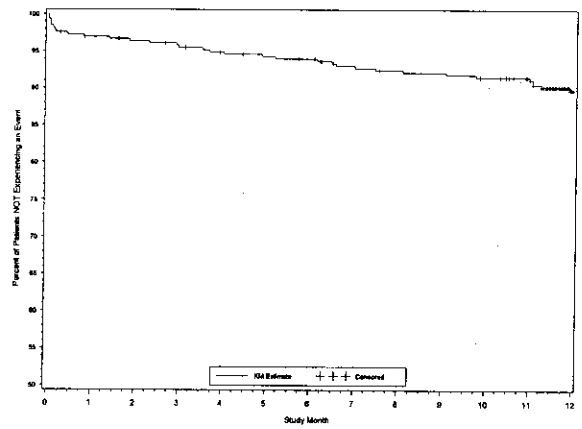


Figure 7: Survival from Major Adverse Events (All Deaths, Strokes and MIs) at 30 Days
Plus Ipsilateral Stroke or Death Related to Ipsilateral Stroke through One Year
Symptomatic Patient Group

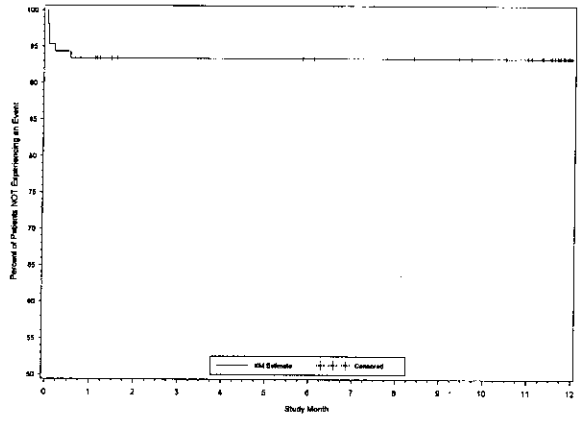
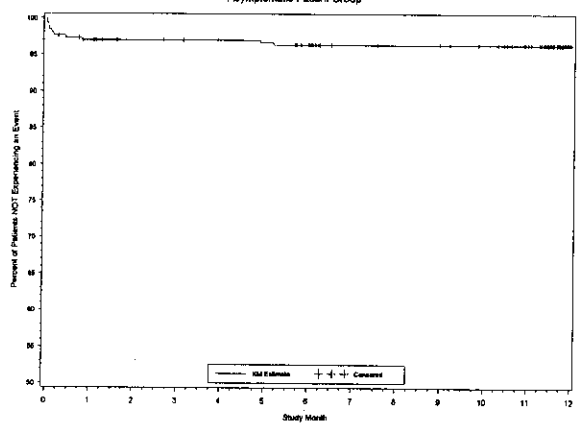


Figure 8: Survival from Major Adverse Events (All Deaths, Strokes and MIs) at 30 Days
Plus Ipsilateral Stroke or Death Related to Ipsilateral Stroke through One Year
Asymptomatic Patient Group



8.0 CLINICIAN USE INFORMATION

WARNING: Do not use after the "Use By" date specified on the package. Assure that the device has been properly stored in a cool, dark, dry place prior to use.

WARNING: The NexStent® System is supplied STERILE and intended for single-use only. Do not use if the package is open or damaged. Do not reuse. Do not resterilize as this can compromise device performance and increase the risk of cross-contamination due to inappropriate reprocessing.

Only physicians who have received appropriate training and are familiar with the principles, clinical applications, complications, side effects and hazards commonly associated with carotid stent placement should use this device.

8.1 Materials Required

- 8F guiding catheter or 6F introducer sheath compatible with the vascular anatomy. Minimum guiding catheter / sheath size inner diameter (I.D.) 0.087in / 2.21mm. Guiding catheter or sheath should not exceed 90cm length.
- The NexStent System is not recommended for use with bleedback control hemostatic valves.
- Balloon dilatation catheter (if required)
- FilterWire EZ™ Embolic Protection System with a 0.014in guidewire (300cm)
- 1,000u / 500cc heparinized normal saline (HepNS) (sterile)
- Two to three 5cc syringes

CAUTION: The NexStent System is not compatible with any guidewire larger than 0.014in (0.36mm).

8.2 Periprocedural Care

During the CABERNET clinical study, the recommended pharmacological treatment included aspirin 325mg b.i.d. and either clopidogrel 75 mg b.i.d. or ticlopidine 250mg b.i.d. was started 48 hours prior to the procedure. After the procedure, recommended guidelines included ticlopidine 250 mg b.i.d. or clopidogrel 75mg daily for four weeks, and aspirin 325mg daily indefinitely. A minimum of 70 units/kg of IV heparin (or other approved anticoagulant) was recommended following sheath insertion to achieve a target ACT of ≥275 seconds or appropriate ACT level as determined by the treating physician. Medication therapy for periprocedural care is at the discretion of the treating physician.

WARNING: Appropriate antiplatelet and anticoagulation therapy should be administered prior to, during and post-procedure.

8.3 Pre-procedure

Refer to Section 9.2 of these instructions for the suggested pre-procedure pharmacological treatment regimen. The placement of the stent in a stenotic or obstructed carotid artery should be done in an angiography procedure room. Angiography should be performed to map out the extent of the lesion(s) and the collateral flow. If thrombus is present, do not proceed with stent deployment. Access vessels must be sufficiently patent or sufficiently recanalized to proceed with further

intervention. Patient preparation and sterile precautions should be the same as for any angioplasty procedure.

8.4 Stent Size Determination

The NexStent® System is intended for use in reference vessel segment diameters between 4mm and 9mm that are <30mm in length.

WARNING: The NexStent System is contraindicated for use with lesions in the ostium of the common carotid artery.

8.5 Inspection Prior To Use

1. Inspect the temperature indicator on the outer box.

WARNING: Do not use if the temperature indicator has exceeded 60°C or has turned from gray to black.

2. Open the outer box and carefully remove the sterile pouch.
3. Before opening sterile pouch seal, inspect for any visible damage such as holes, tears or openings. Do not use the product if any damage to the pouch is detected.
4. Open the sterile pouch and remove the sealed, sterile tray. Inspect the tray for any signs of visible damage such as holes, tears, and openings. Do not use the product if any damage to the tray is detected.
5. Peel open the sterile tray lid and remove the stent/delivery system from the tray and hoop. Examine the device for damage. If it is suspected that the sterility or integrity of the device has been compromised, the device should not be used

CAUTION: Carefully inspect the NexStent System to verify that the device has not been damaged in shipment. Do not use damaged equipment.

6. Inspect the stent through the delivery system sheath to verify that it has not been damaged during shipment and ensure that the stent is fully covered by the sheath.

CAUTION: Special care must be taken not to handle or in any way disrupt the stent on the delivery system. This is most important during catheter removal from packaging, placement over guidewire, and advancement through an RHV and guiding catheter hub.

7. Do not use if any defects are noted.

CAUTION: Do not remove the stent from its delivery system as removal may damage the stent. The stent and the delivery system are intended to perform as a system. If removed, the stent cannot be put back on the delivery system.

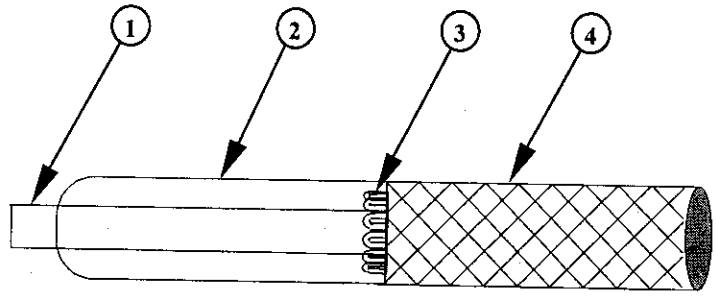
8.6 Preparation

8.6.1 Delivery System Preparation

1. Inspect the system visually to ensure that stent is completely constrained within the delivery system and no damage is observed. Do not use the product if any damage to the system is detected.
2. Prepare a 5cc (ml) syringe with sterile heparinized (3%-5%) saline.
3. Attach the provided stopcock to the Y-connection flush port.

4. Turn the stopcock open to the catheter, and loosen the delivery system RHV. Using the 5cc (ml) syringe, flush the delivery system to purge all the air out of the proximal RHV lumen.
5. Tighten the delivery system RHV and continue to flush until heparinized saline exits from the distal end of the delivery system. Close the stopcock, refill the 5cc (ml) syringe, and reattach it to the stopcock at the Y-connection flush port.
6. Re-prep the 5cc syringe if necessary, and attach to the proximal guidewire lumen flush port. Flush the guidewire lumen until heparinized saline exits from the distal end of the delivery system.
7. Loosen the delivery system RHV. While carefully observing the distal end of the delivery system, slowly rotate the deployment knob counterclockwise to advance the stent to the READY position. See Figure 3. The stent (3) is in the READY position when the green guidewire lumen (1) has advanced out of the clear distal end (2) of the delivery system sheath (4), and the distal edge of the stent is visible within the 5mm clear tip of the delivery system. Stop advancing as soon as the distal edge of the stent is visible within the clear catheter tip.
8. Tighten the delivery system RHV.
9. Evaluate the distal end of the system and verify that the stent is contained within the delivery system sheath as shown in Figure 3. Do not use if the stent is partially deployed or more than halfway across the clear tip section of the catheter.
10. The device is now ready for use.

Figure 3. Stent advanced to the READY position.



8.6.2 Embolic Protection System Preparation

The NexStent® System is indicated for use in conjunction with a FilterWire EZ™ Embolic Protection System. Please refer to the Instructions for Use included with the embolic protection system for information on device preparation and placement.

WARNING: If a filter-based embolic protection system is used, allow for and maintain adequate distance between the filter and the stent delivery system or deployed stent to avoid potential entanglement.

8.6.3 Lesion Preparation

WARNING: Maintain the patient's ACT at >275 seconds throughout the NexStent System and embolic protection system usage to prevent thrombus formation on the device.

CAUTION: Venous access should be available during carotid stenting to manage bradycardia and / or hypotension by either pharmaceutical intervention or placement of a temporary pacemaker, if needed.

CAUTION: The NexStent System must be used with a guiding catheter or introducer sheath to maintain adequate support of the 0.014in guidewire throughout the procedure.

CAUTION: Use with bleedback control hemostatic valves is not recommended.

CAUTION: When catheters are in the body, they should be manipulated only under fluoroscopy. Radiographic equipment that provides high quality images is needed.

WARNING: Maintain continuous flush while removing and reinserting devices on the guidewire. Perform all exchanges slowly to prevent air embolism or trauma to the artery.

1. If needed, pre-dilate the lesion with an appropriate size balloon dilatation catheter to a minimum opening of 4mm.

Note: If no pre-dilatation is performed, there must be a minimum luminal opening of 4mm to enable passage of the stent delivery system.

2. Maintain the guidewire position and withdraw the balloon dilatation catheter.

8.7 Delivery Procedure

CAUTION: Always use a guide catheter/sheath with a hemostasis valve for the implant procedure. An 8F guide catheter or 6F sheath with a minimum I.D. of 0.087in (2.21mm) is recommended.

1. Cross the lesion using a 0.014in (0.36mm) guidewire (or compatible wire-based embolic protection device) with a working length appropriate for use with an Over-the-Wire Stent Delivery System.

NOTE: For use of any embolic protection system, refer to the Directions For Use of that device for warnings, indications, contraindications and proper use techniques.

2. Angiographically verify that the 5F (1.66mm) profile delivery system can cross the target lesion.
3. If required, careful pre-dilation of the lesion may be done using standard practice PTCA techniques with standard balloon catheters with a minimum diameter of 4mm.

CAUTION: Physicians should use judgment based on experience in dilating arterial lesions and/or obstructions. Never force inflation of a balloon catheter to a point that risks dissection of the arterial wall.

8.8 Stent Deployment

WARNING: Ensure optimal positioning of the stent prior to deployment. Once deployment is initiated, the stent cannot be repositioned or recaptured. Stent retrieval methods (use of additional wires, snares and/or forceps) may result in additional trauma to the carotid vasculature and/or the vascular access site. Complications may include death, stroke, bleeding, hematoma, or pseudoaneurysm.

CAUTION: Do not attempt to pull a partially expanded stent back through the guiding catheter or sheath; dislodgement of the stent from the delivery system may occur.

Note: Refer to Figure 2 device diagram

1. Confirm that the RHV on the guide catheter/sheath is locked to prevent any accidental movement of the guidewire.
2. While maintaining guidewire position, backload the NexStent System on to the guidewire by introducing the proximal end of the guidewire into the green distal guidewire lumen (Figure 3. Item 1) of the delivery system.
3. Open the RHV on the guide catheter/sheath. Secure the guidewire and catheter/sheath position. Advance the delivery system over the guidewire distally within the guide catheter/sheath.
4. Under fluoroscopic guidance advance the delivery system until the target lesion is visualized. Advance the delivery system distal to the lesion and pull back the delivery system using the handle to remove slack from the system. The radiopaque marker is located on the inner coil assembly just proximal to the stent. The undeployed stent is visible under fluoroscopy distal to the marker.
5. Tighten the RHV on the guide catheter/sheath to obtain hemostasis, yet continue to allow the delivery system to freely move through the valve.
6. While holding the guide catheter/sheath, adjust the position of the delivery system handle to minimize or eliminate any slack and/or curvature between the catheter/sheath RHV and delivery system handle.
7. Maintain the position of the delivery system handle relative to the patient during stent deployment. Confirm that the stent location is still properly positioned across the target lesion.

CAUTION: Failure to reduce slack and/or curvature of the delivery system catheter between the guide catheter/sheath and delivery system handle during deployment may adversely affect deployment accuracy.

8. Loosen the delivery system RHV. Under fluoroscopic guidance, slowly rotate the deployment control knob counter-clockwise to retract the delivery system, and thus deploy the stent.

CAUTION: If upon initial sheath retraction, the stent delivery system moves relative to the target lesion, discontinue rotating the control knob and re-position the stent delivery system. Once initial stent deployment is visible under fluoroscopy and the stent has made contact with the vessel wall, avoid any additional movement of the delivery system.

9. Continue to slowly rotate the control knob counter-clockwise until the proximal end of the stent is visible under fluoroscopy releasing from the delivery system and expanded to the vessel wall.

CAUTION: If a strong resistance is met with the introduction of the delivery system or difficulty in initiating release of the stent, remove the entire system from the patient and introduce a new NexStent System. Do not use a power injector through the delivery system for angiography.

10. Using fluoroscopic guidance, slowly withdraw the delivery system, and tighten the RHV on the guide catheter/sheath to secure wire position and maintain hemostasis.
11. Using fluoroscopy, visualize the stent to verify full deployment. If further expansion of the stent is desired at any point along the lesion, post-deployment balloon dilatation (standard PTA technique) can be performed.
12. Select an appropriate size PTA balloon catheter and dilate the lesion with standard PTA technique. The inflation diameter of the PTA balloon used for post-dilatation should approximate the diameter of the reference vessel.

CAUTION: Never dilate the stent using a balloon that is larger in diameter than the pre-measured reference vessel diameter.

8.9 Post-Stent Placement

1. Following stent placement, an angiogram should be performed to confirm vessel patency and percent stenosis remaining in the vessel lumen.

WARNING: The stent may cause a thrombus, distal embolization or may migrate from the site of implant down the arterial lumen. Appropriate sizing of the stent to the vessel is required to reduce the possibility of stent migration. In the event of thrombosis of the expanded stent, thrombolysis and PTA should be attempted.

2. Upon completion of the angiogram, the embolic protection system should be removed according to the instructions for use supplied with the device.
3. Patients should be put on an appropriate regimen of anticoagulants / antiplatelets such as that described in Section 8.2.

WARNING: In the event of complications such as infection, pseudoaneurysm, or fistulization, surgical removal of the stent may be required.

WARNING: The long-term performance (>1 year) of the NexStent® Carotid Stent has not been established.

9.0 Storage

Contents supplied STERILE using an ethylene oxide gas process. Non-pyrogenic.

Contents: One (1) NexStent Carotid Stent and Delivery System, one (1) stopcock connector.

Storage: Store in a dry, dark, cool place and do not exceed 60°C. If the package is properly stored, it may be used on or before its expiration date as printed on the package. Rotate inventory so that stents are used prior to the expiration date on package label.

10.0 REUSE PRECAUTION STATEMENT

Do not use if sterile barrier is damaged. If damage is found call your Boston Scientific representative. For single use only. Do not reuse, reprocess or resterilize. Reuse, reprocessing or resterilization may compromise the structural integrity of the device and/or lead to device failure which, in turn, may result in patient injury, illness, or death. Reuse, reprocessing or resterilization may also create a risk of contamination of the device, and/or cause patient infection or cross-infection, including, but not limited to, the transmission of infectious disease(s) from one patient to another. Contamination of the device may lead to injury, illness or death of the patient. After use, dispose of product and packaging in accordance with hospital, administrative and/or local government policy.

11.0 Warranty

EndoTex Interventional Systems, Inc. (EndoTex) warrants that reasonable care has been used in the design and manufacture of this instrument. **This warranty constitutes the entire warranty and is in lieu of and excludes all other warranties not expressly set forth herein, whether expressed or implied by operation of law or otherwise, including, but not limited to, any implied warranties of merchantability or fitness for a particular purpose.** Handling, storage, cleaning and sterilization of this instrument as well as other factors relating to the patient, diagnosis, treatment, surgical procedures, and other matters beyond EndoTex control directly affect the instrument and the results obtained from its use. The product in question must be used according to the Directions for Use, and EndoTex does not warrant this device for in any manner not specified in the Directions for Use. EndoTex's sole obligation under this warranty shall be the repair or replacement of this instrument should it be shown to be defective and EndoTex shall not be liable for any incidental or consequential loss, damage, or expense directly or indirectly arising from the use of this instrument. Any product deemed defective to the satisfaction of EndoTex must be returned to EndoTex for further inspection for this warranty to be operative. EndoTex neither assumes, nor authorizes any other person to assume for it, any other or additional liability or responsibility in connection with this instrument. This instrument must not be reused, reprocessed or resterilized. **EndoTex assumes no liability whatsoever with respect to instruments reused, reprocessed or resterilized and makes no warranties whatsoever, expressed or implied, including but not limited to merchantability or fitness for a particular purpose with respect to such instrument.** In the event that a claim of defect is asserted, submission of such claim must occur with written documentation describing such alleged defect and said alleged defective product must be returned to EndoTex within ninety (90) days of first observation of the alleged defect in order for consideration of this warranty being granted.

Manufactured by:

EndoTex Interventional Systems, Inc.
10231 Bubb Road
Cupertino, CA 95014 USA

Distributed by:

Boston Scientific Corporation
One Boston Scientific Place
Natick, MA 01760-1537
USA
USA Customer Service 888-272-1001

p/n 109-0700
Rev. Draft 10/25/06

Caution: Federal law (USA) restricts this device to sale by or on the order of a physician.

This product contains no detectable Latex.

STERILE EO

For single use only. Do not reuse.

ENDOTEX™
INTERVENTIONAL SYSTEMS

NexStent® Carotid Stent and Monorail® Delivery System

INSTRUCTIONS FOR USE

CAUTION: Federal (USA) law restricts this device to sale by or on the order of a physician.

Limited to use by physicians experienced in carotid stenting and who have received appropriate training in the use of the NexStent Carotid Stent and Monorail Delivery System. The NexStent Carotid Stent and Monorail Delivery System is indicated for use with the FilterWire EZ™ Embolic Protection System.

Manufactured by:

EndoTex Interventional Systems, Inc.
10231 Bubb Road
Cupertino, CA 95014 USA

Distributed by:

Boston Scientific Corporation
One Boston Scientific Place
Natick, MA 01760-1537
USA
USA Customer Service 888-272-1001

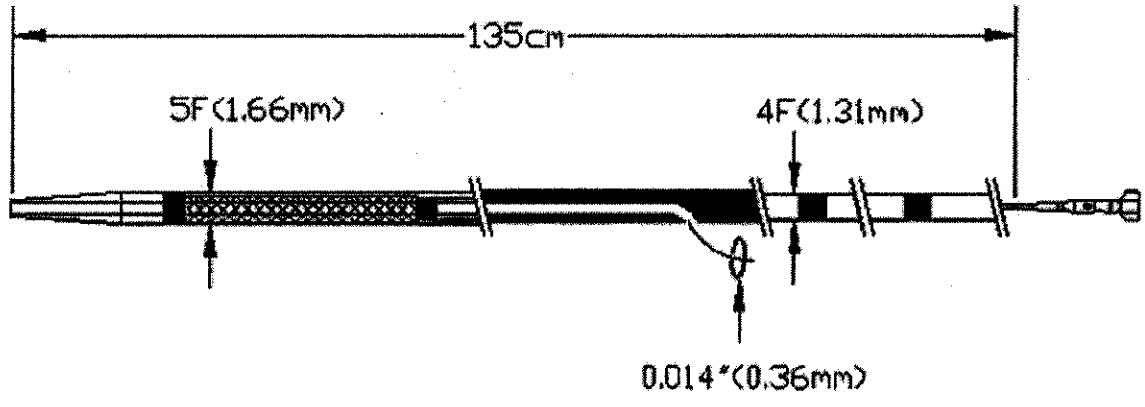
NexStent® Carotid Stent and Monorail® Delivery System
Information for Prescribers

TABLE OF CONTENTS

1.0 DEVICE DESCRIPTION

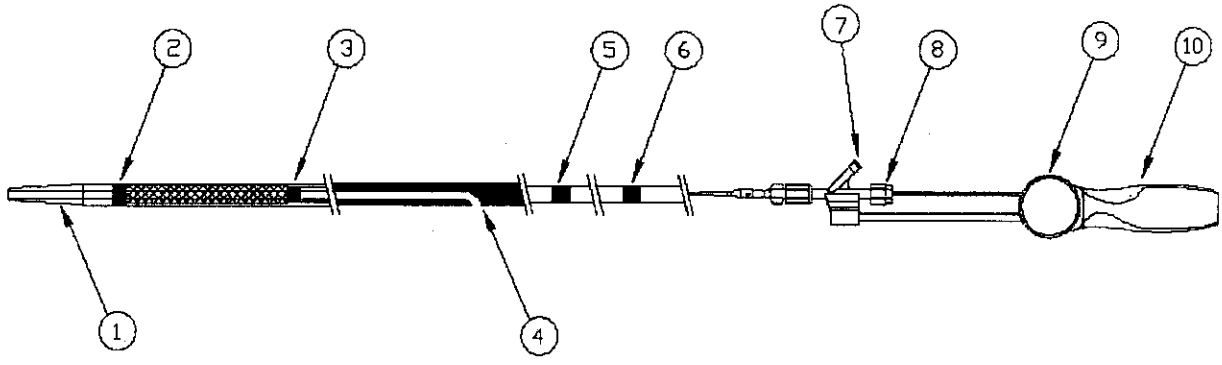
The NexStent® Carotid Stent and Monorail® Delivery System is intended to deliver a self-expanding stent to the extra-cranial carotid arteries via a sheathed percutaneous Monorail delivery system. The NexStent carotid stent is a flexible, self-expanding, rolled Nitinol (nickel-titanium alloy) mesh. One stent size is used for treating vessel diameters ranging from 4mm to 9mm. The length of the stent is 33mm in the delivery system and is approximately 30mm at a fully deployed diameter of 9mm. The stent is constrained within a 5F (1.66mm) Outside Diameter (O.D.) delivery system as shown in Figure 1. Upon deployment into the carotid vasculature, the stent expands to the vessel diameter, imparting an outward radial force on the vessel wall to establish and maintain vessel patency.

Figure 1 Delivery System Schematic



The general features of the NexStent Monorail System are shown in Figure 2. The delivery system has a radiopaque tracking tip (1) to facilitate delivery system tracking through the carotid arterial vasculature. The stent is located at the distal end of the delivery system catheter between two radiopaque markers, the distal stent location marker (2) and the proximal stent location marker (3). The delivery system is a rapid exchange system compatible with standard 0.014in (0.36mm) or smaller guidewires. The delivery system has a proximal guidewire exit port (4) that is located approximately 25cm from the distal end of the tracking tip. The delivery sheath has two marker bands, located on the outside of the delivery system catheter shaft, at 90cm (5) and 100cm (6) from the tracking tip, to assist the operator in visualizing catheter advancement. The delivery system has a Y-connection flush port (7) located distal to a rotating hemostasis valve (RHV) (8). The control knob (9) and delivery handle (10) controls the relative position of the sheath and stent during stent delivery.

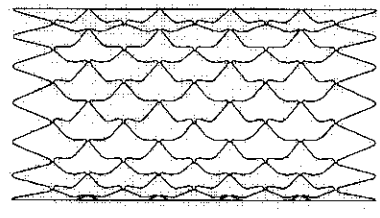
Figure 2 Delivery System Schematic



The NexStent® Monorail® System is available in a single 30mm stent length that accommodates reference vessel diameters between 4mm and 9mm. The NexStent adapts to both straight and tapered vessel anatomies. See Table 1 for recommended reference vessel diameter.

The NexStent Monorail System is compatible with either an 8F guiding catheter or a 6F introducer sheath (min. ID 0.087in / 2.21mm). It is also compatible with the FilterWire EZ™ Embolic Protection System.

Table 1. NexStent Carotid Stent



Stent Length (mm)	Reference Vessel Diameter (mm)
30	4.0-9.0

2.0 INDICATIONS FOR USE

The NexStent® Monorail® System used in conjunction with the Filter Wire EZ™ Embolic Protection System, is indicated for treatment of patients at high risk for adverse events from carotid endarterectomy (See Section 8 of these instructions) who require carotid revascularization and meet the criteria outlined below:

1. Patients with neurological symptoms associated with ≥50% stenosis of the common or internal carotid artery OR patients without neurological symptoms and ≥80% stenosis of the common or internal carotid artery by ultrasound or angiogram **AND**
2. Patients must have a reference vessel diameter within the range of 4mm and 9mm at the target lesion and a stenosis less than 30mm in length.

3.0 CONTRAINDICATIONS

The NexStent System is contraindicated for use in:

- Patients in whom anticoagulant and/or antiplatelet therapy is contraindicated.
- Patients with severe vascular tortuosity or anatomy that would preclude the safe introduction of the Guiding Catheter/ Sheath, , Embolic Protection System, Delivery Catheter, and/or Retrieval Catheter.
- Patients with a known hypersensitivity to nickel-titanium.
- Patients with uncorrected bleeding disorders.
- Lesions in the ostium of the common carotid artery.

4.0 WARNINGS

WARNING: Only physicians who have received appropriate training and are familiar with the principles, clinical applications, complications, side effects and hazards commonly associated with carotid interventional procedures should use this device.

General

Refer to the Instructions for Use supplied with any interventional device to be used in conjunction with the NexStent Monorail System for intended uses, contraindications, and potential complications.

The safety and efficacy of the NexStent Monorail System has not been demonstrated with embolic protection systems other than the FilterWire EZ Embolic Protection System.

The long-term performance (>1 year) of the NexStent Carotid Stent has not been established.

As with any type of vascular implant, infection secondary to contamination of the stent may lead to thrombosis, pseudoaneurysm, or rupture.

Stenting across a major bifurcation may limit access for future diagnostic or therapeutic procedures.

In patients requiring the use of antacids and/or H2-antagonists before or immediately after stent placement, oral absorption of antiplatelet agents (e.g. aspirin) may be adversely affected.

Only physicians who have received appropriate training and are familiar with the principles, clinical applications, complications, side effects and hazards commonly associated with carotid stent placement should use this device.

Appropriate antiplatelet and anticoagulation therapy should be administered pre- and post-procedure as suggested in these instructions. Special consideration should be given to those patients with recently active gastritis or peptic ulcer disease or other bleeding disorders.

When multiple stents are required, stent materials should be of similar composition.

The Safety and Effectiveness of the NexStent Carotid Stent System has NOT been established in patients with the characteristics noted below.

- Treatment of carotid lesions in patients with carotid artery disease who are not at high risk for carotid endarterectomy.
- Previously placed stent in target artery.
- Total occlusion of the target lesion.
- Angiographic visible thrombus.
- Carotid string sign (a tiny, long segment of contrast in the true lumen of the artery).
- Vessel anatomy precluding the use of the stent system or appropriate positioning of the embolic protection system.
- Presence of carotid artery dissection prior to initiation of the procedure.
- Evidence of a stroke within the previous 30 days.
- History of ipsilateral stroke with fluctuating neurologic symptoms within 1 year.
- History of intracranial hemorrhage within the past 3 months.
- Any condition that precluded proper angiographic assessment or made percutaneous arterial access unsafe, (e.g. morbid obesity, sustained systolic blood pressure >180 mmHg).
- Contraindication to aspirin, or to clopidogrel AND ticlopidine, or stent material.
- History or current indication of bleeding diathesis or coagulopathy including thrombocytopenia or an inability to receive heparin in amounts sufficient to maintain an activated clot time at >250 seconds.
- Hemoglobin (Hgb) <8gm/dl (unless on dialysis), platelet count < 50,000, INR > 1.5 (irreversible), or heparin-associated thrombocytopenia.
- Known cardiac sources of emboli.
- Atherosclerotic disease involving adjoining vessels precluding safe placement of the guiding catheter or sheath.
- Other abnormal angiographic findings that indicated the patient was at risk of a stroke due to a problem other than that of the target lesion, such as: ipsilateral arterial stenosis greater in severity than the target lesion, cerebral aneurysm, or arteriovenous malformation of the cerebral vasculature.
- Severe dementia.
- Life threatening allergy to contrast media that could not be treated.
- Pregnant patients or patients under the age of 18.
- Patients in whom femoral access is not possible.
- Patients with aneurysmal dilation immediately proximal or distal to the lesion.

The safety and effectiveness of concurrent treatment of lesions in patients with bilateral carotid artery disease have not been established.

Device Use

- This device is intended for single-use only. DO NOT reuse. DO NOT resterilize, as this can compromise device performance and increase the risk of cross contamination due to inappropriate reprocessing.
- Do not use the product after the "Use By" date specified on the package.
- Do not use the product if temperature exposure has exceeded 60°C or if the indicator on the box has turned from light gray to black.
- Maintain the patient's Activated Clotting Time (ACT) at >275 seconds throughout the NexStent® Monorail® System and distal protection usage to prevent thrombus formation on the devices.
- Maintain continuous flush while removing and reinserting devices on the guidewire. Perform all exchanges slowly to prevent air embolism or trauma to the artery.
- Implanting a stent may lead to dissection of the vessel distal and/or proximal to the stent and may cause acute closure of the vessel, requiring additional intervention (carotid endarterectomy, further dilatation, or placement of additional stents).
- The stent may cause a thrombus, distal embolization or may migrate from the site of implant down the arterial lumen. Appropriate sizing of the stent to the vessel is required to reduce the possibility of stent migration. In the event of thrombosis of the expanded stent, thrombolysis and PTA should be attempted.
- In the event of complications such as infection, pseudoaneurysm or fistulization, surgical removal of the stent may be required.
- Overstretching of the artery may result in rupture and life-threatening bleeding.
- If a filter-based embolic protection system is used, allow for and maintain adequate distance between the filter and the stent delivery system or deployed stent to avoid potential entanglement.
- Ensure optimal positioning of the stent prior to deployment. Once deployment is initiated, the stent cannot be repositioned or recaptured. Stent retrieval methods (use of additional wires, snares and/or forceps) may result in additional trauma to the carotid vasculature and/or the vascular access site. Complications may include death, stroke, bleeding, hematoma or pseudoaneurysm.

5.0 PRECAUTIONS

5.1 Stent Handling – Precautions

Carefully inspect the NexStent Monorail System to verify that the device has not been damaged in shipment.

Do not use damaged equipment. Take care to avoid unnecessary handling, which may kink or damage the delivery system.

Do not use if device is kinked.

Do not use if the stent is partially deployed.

Do not expose the delivery system to organic solvents (e.g. alcohol) as structural integrity and/or function of the device may be impaired.

Do not remove the stent from its delivery system as removal may damage the stent. The stent and the delivery system are intended to perform as a system. If removed, the stent cannot be put back in the delivery system.

Precautions to prevent or reduce clotting should be taken when any interventional device is used. Flush or rinse all devices entering the vascular system with sterile isotonic heparinized saline prior to use.

The delivery system should not be used in conjunction with other stents. Special care must be taken not to handle or in any way disrupt the stent in the delivery system.

5.2 Stent Placement - Precautions

Use with bleed-back control hemostatic valves is not recommended.

The NexStent® Monorail® System is not compatible with any guidewire larger than 0.014in (0.36mm).

The NexStent Monorail System must be used with a guiding catheter or introducer sheath to maintain adequate support of the 0.014in guidewire throughout the procedure.

For best device performance, the guidewire exit port should remain within the guiding catheter or sheath.

Do not attempt to reposition the Delivery System once the stent has made contact with the vessel wall.

Ensure the stent system is fully flushed with heparinized saline prior to use. Do not use the delivery system if flush is not observed exiting at the distal end of the sheath.

Do not attempt to pull a partially expanded stent back through the guiding catheter or sheath; dislodgment of the stent from the delivery system may occur.

Venous access should be available during carotid stenting to manage bradycardia and / or hypotension by either pharmaceutical intervention or placement of a temporary pacemaker, if needed.

When catheters are in the body, they should be manipulated only under fluoroscopy. Radiographic equipment that provides high quality imaging is needed.

The delivery system is not designed for use with power injection. Use of power injection may adversely affect device performance.

If resistance is met during delivery system introduction, the system should be withdrawn and another system used.

Prior to stent deployment, remove all slack from the delivery system.

5.3 Post-Implant – Precautions

Care must be exercised when crossing a newly deployed stent with other interventional devices to avoid disrupting the stent geometry and placement of the stent. In the event of thrombosis of the expanded stent, thrombolysis and PTA should be attempted.

If more than one stent is required to cover the lesion or if there are multiple lesions, the distal lesion would be stented first, followed by stenting of the proximal lesion.

If overlap of sequential stents is necessary, the amount of overlap should be kept to a minimum. An overlap of 5mm is generally considered acceptable.

5.3.1 Length of Follow up / Special Patient Populations

The safety and efficacy of the NexStent® Carotid Stent beyond 12 months of follow up has not been established in patients that are at high risk for carotid endarterectomy.

5.3.2 Magnetic Resonance Imaging (MRI) Compatibility

- Non-clinical testing of the NexStent Carotid Stent has shown it to be MRI safe at field strengths of 3.0 Tesla or less and a whole body averaged specific absorption rate (SAR) of 2.0 W/kg and special peak SAR of 4.0 W/kg at a maximum MRI exposure of 15 minutes. This level of exposure to radiofrequency (RF) exceeds that typically used for clinical MRI procedures.
- Non-clinical testing has shown that, with a stent orientation of 45 degrees to the angle of the MRI field, stent migration is unlikely to occur in environments of 3.0 Tesla.
- Non-clinical testing has been performed to ensure the stent produced a temperature rise of less than or equal to 0.2°C. The imaging parameters produced an MRI system reported value for the whole body averaged SAR of 2.0 W/kg and special peak SAR of 4.0 W/kg at a maximum MR exposure of 15 minutes.
- The effect of heating in the MRI environment for overlapping stents or stents with fractured struts is not known.
- MRI quality may be compromised if the area of interest is in the exact same area as or relatively close to the position of the stent.

6.0 ADVERSE EVENTS

6.1 Observed Adverse Events

In the CABERNET trial, the NexStent Carotid Stent and Delivery System (OTW) was evaluated for the treatment of patients with significant extracranial carotid artery stenosis who required carotid revascularization and were at high risk for adverse events from carotid endarterectomy. A total of 454 patients were enrolled in the main registry of the trial.

The primary endpoints of the trial were:

1. Major clinical events at one-year defined as any death, stroke or myocardial infarction (MI).

2. Thirty-day event rate defined as any death, stroke or MI ≤30 days post-procedure; plus the 31-day to 12-month event rate defined as any ipsilateral stroke including any death as a result of an ipsilateral stroke.

The primary objective of the trial was to demonstrate that the major adverse event (MAE) rates for both primary endpoints were not inferior to an Objective Performance Criteria (OPC) derived from the MAE rate historically associated with carotid endarterectomy (CEA).

Tables 2 and 3 present the MAE and the serious adverse events (SAE) reported for the enrolled patients through 1 year. Table 4 presents the patient deaths by causation. The major adverse events table summarizes all deaths, strokes and MIs.

TABLE 2. Major Adverse Events

Major Adverse Events	≤30 days (n=438) [1]		31-365 days (n=421) [2]		Cumulative 0-365 Days (n=421) [2]	
Primary Endpoints	# Patients	%	# Patients	%	# Patients	%
All Death Stroke and MI at 1 Yr.	17	3.9	33	7.8	50	11.9 [4]UCL=14.8 %
	# Patients	%Patients (N=438)	# Patients	% Patients (N=404)[3]	# Patients	% Patients (N=404)[3]
All Death Stroke and MI ≤ 30 days; plus the 31-day to12-month event rate defined as any ipsilateral stroke including any death as a result of an ipsilateral stroke	17	3.9	3	0.7	19	4.7 UCL=6.8%
Major Adverse Events by Classification	≤30 days (n = 438)		31-365 days (n = 421) [2]		Cumulative 0-365 Days (n = 421) [2]	
	# Patients	%	# Patients	%	# Patients	%
Death	2	0.5	17	4.0	19	4.5
Stroke	15	3.4	8	1.9	21	5.0
Ipsilateral Stroke	12	2.7	3	0.7	14	3.3
Major	5	1.1	1	0.2	5	1.2
Minor	7	1.6	2	0.5	9	2.1
Non-Ipsilateral Stroke	3	0.7	6	1.4	8	1.9
Major	1	0.2	3	0.7	4	1.0
Minor	2	0.5	3	0.7	4	1.0
Myocardial Infarction (MI)	1	0.2	16	3.8	17	4.0

[1] N= Patients enrolled in main trial registry (N=454) less patients not stented (N= 11), patients lost to follow-up at 30-day evaluation period (N=3) and patients who had a missed visit at the 30-day timepoint (N=2)

[2] N=421 for the 31-365 and 0-365 time periods. This includes 398 patients evaluated at 1 year, 19 deaths, and 4 patients that did not have a 1-year visit but experienced an adverse event (398+19+4 = 421).

[3] In an effort to present the most conservative analysis for the MAE rate concerning the composite Primary Endpoint N=404 was used. Seventeen patient deaths that occurred during the 31-365 day time period were not due to ipsilateral stroke and were excluded from this analysis. Therefore N = 404 (421-17=404).

[4] Upper Confidence Limit

TABLE 3. Serious Adverse Events

Event Categories[1]	≤ 30 days (N = 454)		31-365 days (N =443)		0-365 Days (N =454)	
	# Patients	% Patients	# Patients	% Patients	# Patients	% Patients
Procedure Related						
Angina	3	0.7	0	0.0	3	0.7
Bleeding/Anemia[2]	16	3.5	1	0.0	17	3.7
Cardiac Dysrrhythmia	14	3.1	0	0.0	14	3.1
Cardiogenic Shock	1	0.2	0	0.0	1	0.2
Ischemia/ ↑ Enzymes	4	0.9	0	0.0	4	0.9
Syncope	4	0.9	0	0.0	4	0.9
Cerebrovascular	3	0.7	0	0.0	3	0.7
Emergent CEA	1	0.2	0	0.0	1	0.2
Genitourinary	1	0.2	0	0.0	1	0.2
Hypotension	19	4.2	0	0.0	19	4.2
Hypertension	1	0.2	0	0.0	1	0.2
Infection	3	0.7	0	0.0	3	0.7
Metabolic	5	1.1	0	0.0	5	1.1
Musculoskeletal	2	0.4	0	0.0	2	0.4
Neurological	11	2.4	0	0.0	11	2.4
Prolonged Hospitalization	1	0.2	0	0.0	1	0.2
Respiratory	2	0.4	0	0.0	2	0.4
Vascular	7	1.5	5	1.1	12	2.6
Other	2	0.4	0	0.0	2	0.4
Access Site Complications[3]						
Bleeding and Hematoma	9	2.0	0	0.0	9	2.0
Ecchymosis	1	0.2	0	0.0	1	0.2
Pseudoaneurysm	3	0.7	1	0.2	4	0.9
Poss. Femoral Artery Thrombosis	1	0.2	0	0.0	1	0.2
Wound Infection	2	0.4	0	0.0	2	0.4
Total Procedure related	80	17.6	7	1.6	85	18.7
Non-Procedure Related						
Cardiac						
Angina	2	0.4	20	4.5	22	4.8
Cardiogenic Shock	0	0.0	1	0.2	1	0.2
Congestive Heart Failure (CHF)	3	0.7	16	3.6	19	4.2
Coronary Artery Disease	2	0.4	26	5.9	28	6.2
Dysrrhythmia	2	0.4	12	2.7	14	3.1
Ischemia/ ↑ Enzymes	3	0.7	3	0.7	5	1.1
Syncope	1	0.2	1	0.2	1	0.2
Valvular Disease	0	0.0	5	1.1	5	1.1
Other	1	0.2	2	1.1	3	0.7
Neurological						
TIA	0	0.0	8	1.8	8	1.8
Altered Mental Status	1	0.2	2	0.5	3	0.7
Organic Brain	0	0.0	2	0.5	2	0.4

Event Categories[1]	≤ 30 days (N = 454)		31-365 days (N =443)		0-365 Days (N =454)	
	# Patients	% Patients	# Patients	% Patients	# Patients	% Patients
Syndrome/Memory Loss						
Seizure	1	0.2	2	0.5	3	0.7
Syncope/Dizziness	1	0.2	11	2.5	12	2.6
Visual Disturbance	0	0.0	2	0.5	2	0.4
Other	0	0.0	1	0.2	1	0.2
Other Systems						
Bleeding	2	0.4	8	1.8	10	2.2
Blood Dyscrasia	9	2.0	9	2.0	17	3.7
Carcinoma	1	0.2	9	2.0	10	2.2
Cerebrovascular	0	0.0	5	1.1	5	1.1
Gastrointestinal	6	1.3	30	6.8	35	7.7
Genitourinary	3	0.7	1	0.2	4	0.9
Hemodynamic	2	0.4	7	1.6	9	2.0
Infection	2	0.4	10	2.3	12	2.6
Metabolic	2	0.4	10	2.3	12	2.6
Musculoskeletal	1	0.2	13	2.9	14	3.1
Other Hospitalization	0	0.0	22	5.0	22	4.8
Respiratory	2	0.4	18	4.1	19	4.2
Vascular[4]	4	0.9	42	9.5	45	9.9
Other	6	1.3	7	1.6	11	2.4
Total Non-Procedure Related	46	10.1	186	42.0	206	45.4

[1] Patients may have had multiple events and therefore can be counted in more than one category/subcategory of event. Counts represent the number of patients who have experienced one or more events.
[2] Twenty patients that had procedure related bleeding (non-access site) required a blood transfusion; 14 of the 20 events were procedure related
[3] Six access site complications required blood transfusions.
[4] Three of the 9 patients reported as having restenosis are not included in the "Vascular" event category secondary to AE forms which were pending for "target lesion restenosis"; however the 3 patients are reported in the secondary endpoint for restenosis.

Events are categorized by body system and are defined as follows:

- Access site includes such events as aneurysm, bleeding, bruising or ecchymosis, hematoma, pseudo-aneurysm, pain and arterial thrombosis.
- Bleeding includes such non access-site bleeding, nose bleed, surgical or incisional bleeding and retroperitoneal bleed.
- Blood Dyscrasia includes events such as anemia, thrombocytopenia, and leucopenia.
- Carcinoma includes such events as lung cancer, breast cancer, leukemia, brain tumor, rectal cancer.
- Cardiac includes such events as angina, coronary artery disease, cardiac dysrrhythmia, congestive heart failure cardiac-related syncope and valvular disease (aortic and mitral).
- Cerebrovascular includes such events as headache and brain hemorrhage.
- Gastrointestinal includes events such as dysphagia, indigestion, nausea, vomiting, esophageal stenosis or varicies, ulcer, bowel obstruction, GI Bleed, colitis, cholecystitis, pancreatitis, hepatic disorders, diverticulitis, melena and rectal prolapse.

- Genitourinary includes events such as urinary retention, hematuria, nocturia related to prostatic hyperplasia and lower abdominal pain related to the bladder or prostate.
- Hemodynamic includes events such as hypotension and hypertension
- Metabolic includes events such as diabetes, dehydration, electrolyte imbalance and renal failure.
- Musculoskeletal includes events such as bone, muscle or joint pain, fractures and arthritis injury, and inguinal hernia.
- Infection includes events such as conjunctivitis, cellulitis, parotitis, abscess, system infection, sepsis, fungal infection, urinary tract infection, wound infection and non-specified infection.
- Neurological includes all non-stroke related events such as altered mental status/confusion/dementia/organic brain syndrome, seizure, sensory deficits (peripheral numbness or weakness), visual/speech disturbances, neurologic-related syncope or dizziness, and TIA.
- Respiratory includes events such as pneumonia, hemoptysis, respiratory. failure and chronic obstructive lung disease.
- Vascular includes such as events as carotid restenosis (target and non-target lesion), peripheral arterial disease, and peripheral arterial or venous thrombosis.
- Other Hospitalizations include hospitalizations for other medical/surgical treatment.
- Other is a miscellaneous category that includes such events as agitation, drug hypersensitivity, patient fall (non-neurologic) rash, general weakness, gout, peripheral edema, fatigue etc.

TABLE 4. Patient Deaths

Event Categories	Total (n=421)	
	Deaths	%
0-30 days		
Cardiac	1	0.2
Sepsis	1	0.2
31-365 days		
Cardiac	9	2.1
Carcinoma	2	0.5
Respiratory	2	0.5
Gastrointestinal	1	0.2
Renal Failure	1	0.2
Liver Failure	1	0.2
Unknown	1	0.2
Total Deaths (0-365 days)	19	4.5

Note: There were no neurologic related deaths

6.2 Potential Adverse Events

Based on the literature and on clinical and commercial experience with carotid stents and embolic protection systems, the following alphabetical list includes possible adverse events associated with use of these devices:

- Allergic reactions to anti-platelet agents/contrast medium
- Aneurysm
- Angina/coronary ischemia
- Arrhythmia
- Arterial occlusion/thrombosis at puncture site or remote site
- Arteriovenous fistula
- Bacteremia or septicemia
- Bleeding from anticoagulant or antiplatelet medications
- Cerebral edema
- Cerebral hemorrhage
- Cerebral ischemia/transient ischemia attack (TIA)
- Congestive heart failure (CHF)
- Death
- Detachment and/or implantation of a component of the system
- Emboli, distal (air, tissue or thrombotic emboli)
- Emergent or urgent endarterectomy surgery (CEA)
- Fever
- Filter thrombosis/occlusion
- Groin hematoma, with or without surgical repair
- Hemorrhage, with or without transfusion
- Hyperperfusion syndrome
- Hypotension/hypertension
- Infection and pain at insertion site
- Ischemia/infarction of tissue/organ
- Myocardial infarction (MI)
- Pain (head, neck)
- Pseudoaneurysm, femoral
- Renal failure/insufficiency
- Restenosis of stented segment
- Seizure
- Severe unilateral headache
- Stent/filter entanglement/damage
- Stent embolization
- Stent malposition
- Stent migration
- Stent thrombosis/occlusion
- Stroke/cerebrovascular accident (CVA)
- Total occlusion of carotid artery
- Vessel dissection, perforation, or rupture
- Vessel spasm or recoil

Any device related adverse event occurring involving the NexStent® Carotid Stent System should be reported immediately to Boston Scientific Corporation at (888) 272-1001.

7.0 CABERNET Trial

The Carotid Artery Revascularization Using the Boston Scientific EPI FilterWire EX/EZ system and the EndoTex NexStent (CABERNET Trial) was a prospective, non-randomized multicenter clinical trial evaluating the safety and efficacy of the NexStent Carotid Stent and Delivery System (NexStent) in conjunction with the Boston Scientific FilterWire EX System and EZ System. The CABERNET study protocol included implantation of the NexStent for the treatment of patients with significant extracranial carotid artery stenosis who required carotid revascularization and were at high risk for adverse events from carotid endarterectomy. An overview of the clinical trial is provided in Table 5. High risk for carotid endarterectomy was established with anatomical and co-mordid conditions. The study was designed to demonstrate an adverse event rate not greater than the historical control (12.1%) plus an additional delta of 4% established for this study (16.1%).

Table 5. CABERNET Trial Overview

Title:	Carotid Artery Revascularization Using the Boston Scientific FilterWire EX/EZ System and the EndoTex NexStent.
Products Evaluated	EndoTex NexStent in conjunction with Boston Scientific FilterWire EX System or EZ System System.
Study Design:	A prospective, non-randomized, multicenter clinical trial.
Clinical Sites:	A total of 21 Sites participated in the trial. At two sites the study was transitioned to other institutions. Of the remaining 19 sites, there were 15 US sites and 4 OUS sites.
Primary Endpoints[6]:	**Safety** 1) Major clinical events at one-year defined as any death, stroke or myocardial infarction 2) 30-day event rate defined as any death, stroke or MI ≤ 30-days post-procedure; plus the 31-day to12-month event rate defined as any ipsilateral stroke including any death as a result of an ipsilateral stroke.
Secondary Endpoints:	**Safety and Efficacy** NexStent Technical Success[1] FilterWire Technical Success[1] Overall System Technical Success[1] Angiographic Success[2] Procedure Success[3] Restenosis [4] Target Vessel Revascularization[5]
Study Hypothesis	Non-Inferiority compared to a historical control for patients at high risk for CEA.
Patient Follow-up	Follow-up Visits: Hospital Discharge, 1-Month, 6-Month, 12-Month, 2-Year, 3-Year.

[1]Technical Success rates were based on the devices being placed and retrieved as described in the study protocol.
[2]Angiographic Success was achievement of ≤50% residual stenosis based on the original diameter of the target lesion.
[3]Procedural Success was defined as patients who had angiographic success, overall system success and MAE free within 24 hours of the index procedure.
[4]Restenosis was defined >80% narrowing of the target lesion based on the Strandness criteria that occurred >1 month post procedure.
[5]Target Vessel Revascularization was defined as any narrowing of the target lesion or vessel >1 month post procedure, requiring revascularization.
[6]The primary endpoints of the trial were evaluated at 1 year.

The primary endpoints of the trial were:

1. Major clinical events at one-year defined as any death, stroke or myocardial infarction (MI).
2. Thirty day event rate defined as any death, stroke or MI ≤30-days post-procedure; plus the 31-day to12-month event rate defined as any ipsilateral stroke including any death as a result of an ipsilateral stroke.

The primary objective of the trial was to demonstrate that the major adverse event (MAE) rates for both primary endpoints were not greater than the MAE events rates associated with high-risk carotid endarterectomy (12.1%) plus an additional delta of 4% established for this study (16.1%).

The study hypotheses were compared to a historical control for adverse events occurring in high-risk patients undergoing carotid endarterectomy (11% for anatomical risk factor and 14% for comorbidity), plus a statistical equivalence delta of 4 percentage points. The weighting factors for the adjusted adverse event rate (OPC) were determined by the observed case mix of anatomical high-risk patients vs. co-morbid high-risk patients in this patient sample.

The null hypothesis of study device system inferiority to control was tested against the alternative hypothesis of equivalence (non-inferiority) to control.

H_0: $P \geq OPC + 0.04$
H_a: $P < OPC + 0.04$

The hypotheses were tested by calculating a normal approximation to the binomial test statistic, Z. If $Z > Z_{0.05} = 1.645$ (the weighted OPC plus equivalence threshold) then the null hypothesis of inferiority will be rejected and the study device system was considered equivalent to CEA.

Patients were followed at hospital discharge, 1-Month, 6-Months, and 1-Year. Additionally, registry patients will be followed annually through 3 years from the date of the index procedure. Patients were seen in follow-up by the treating physician as well as independent neurologist (neurological assessments). Core laboratories were utilized for the analysis of angiographic, ultrasound, ECG and CT/MRI (only for evaluation of neurological events or symptomology) data. To ensure patient safety, medical monitors reviewed safety data to ensure appropriate reporting of adverse events.

A Clinical Events Committee (CEC) reviewed all reported major adverse events for the primary endpoint and a Data Safety Monitoring Board (DSMB) reviewed the summary of these events to ensure patient safety.

Inclusion Criteria The study population consisted of male and female patients, at least 18 years of age, with discrete lesions in the internal or common carotid artery or the carotid bifurcation. Patients had to be high-risk candidates for carotid endarterectomy (CEA); both symptomatic (≥50% stenosis) and asymptomatic (≥60% stenosis by angiography, 80% stenosis by ultrasound) patients were eligible.

Key inclusion criteria included the following:

- Lesion is located in the common carotid artery (CCA) and/or the internal carotid artery (ICA) or the carotid bifurcation.
- Target vessel is the only vessel being treated at this intervention and the lesion is ≤30mm and can be treated with a single stent.
- Vessel to be treated is between 4mm and 9mm in diameter.
- Distal vessel "landing zone" for placement of the FilterWire must be between 3.5 mm and 5.5mm in diameter and have available the following artery lengths:
  - A minimum of 2.0cm distal to the target lesion.
  - A minimum of 2.0cm straight vessel segment for placement of the filter.
  - A minimum of 1.0cm from a major vessel curve.

Patients were required to meet one of the following criteria:

- **Symptomatic:** Stenosis must be ≥50% as determined by duplex ultrasound and angiogram; and the patient has a history of stroke, TIA and/or amaurosis fugax in the hemisphere supplied by the target vessel within 180 days of the procedure.

OR

- **Asymptomatic:** Stenosis must be ≥80% as determined by duplex ultrasound and ≥60% as determined by angiogram without any neurological symptoms.

Eligible patients were required to meet at least one of the following high risk anatomical conditions, one of the Class I high risk comorbid conditions or two of the Class II high risk comorbid conditions criteria in order to be eligible to participate in the study:

Anatomical High-Risk Conditions

1. Previous carotid endarterectomy with significant restenosis (as defined above for symptomatic or asymptomatic patients).
2. Total occlusion of the contralateral carotid artery.
3. Previous radiation treatment to the neck or radical neck dissection.
4. Target lesion is at or above the second vertebral body (C2) or below the clavicle.
5. Inability to extend the head due to cervical arthritis or other cervical disorders.
6. Tracheostomy or tracheal stoma.
7. Presence of laryngeal nerve palsy.
8. Bilateral carotid artery stenosis as determined by angiography in which both carotid arteries require treatment, as defined as:
   a. Bilateral asymptomatic stenosis ≥60% or,
   b. Bilateral symptomatic stenosis ≥50% or,
   c. Bilateral stenoses, one side with a symptomatic stenosis ≥50% and the other side asymptomatic with a stenosis ≥60%.

Comorbid High-Risk Conditions

CLASS I HIGH RISK (Only one of the following were required)

1. Unstable angina (rest pain with ECG changes).
2. Known severe left ventricular dysfunction, LVEF <30%.
3. Congestive heart failure (CHF) - New York Heart Association Functional Class III or IV.
4. Dialysis dependent renal failure.
5. Chronic Obstructive Pulmonary Disease(COPD) with either: Forced Expiratory Volume in 1 Second (FEV1) <50% predicted or, Chronic oxygen therapy or, Resting PO2 of ≤60 mmHg or, baseline hematocrit ≥50%.
6. Requirement for staged CABG or valve replacement post carotid index procedure.

CLASS II HIGH RISK (Two of the following were required)

1. Patient is ≥75 years of age.
2. Myocardial infarction within previous 6 weeks.
3. Requires staged peripheral vascular surgery (i.e. abdominal aortic aneurysm repair) or other major surgery post carotid index procedure.
4. Two or more proximal or major diseased coronary arteries with ≥70% stenosis that have not or cannot be revascularized.

Exclusion Criteria

A patient with any of the following criteria was not considered eligible for treatment in the trial.

1. Previously placed stent in target vessel.
2. Total occlusion of target vessel (ICA or CCA).
3. Angiographically visible thrombus.
4. Carotid string sign (a tiny, long segment of contrast in the true lumen of the artery, aneurysmal pouch formation, and the distal location of the arteriopathy) with poor visualization of the distal vessel.
5. Vertebrobasilar insufficiency symptoms only, without clearly identifiable symptoms referable to the targeted carotid artery.
6. Vessel anatomy precluding use of stent system or distal protection system.
7. Presence of carotid artery dissection.
8. Requirement for staged CABG, valve replacement or abdominal aortic aneurysm procedure ±30 days of the index procedure.
9. Evidence of a major disabling stroke within the previous 30 days.
10. Patient has an evolving stroke or has experienced a major stroke (NIHSS score ≥15) within 3 months.
11. History of intracranial hemorrhage within the past 12 months.
12. Any condition that precludes proper angiographic assessment or makes percutaneous arterial access unsafe, e.g. morbid obesity, history of chronic hypertension that is not controlled by medical therapy.
13. Contraindication to heparin, aspirin, clopidogrel (Plavix®), X-ray contrast or ticlopidine (Ticlid®) in cases of intolerance to clopidogrel.

14. History of liver failure with elevated prothrombin time.
15. History or current indication of bleeding diathesis or coagulopathy.
16. Hgb <8gm/dl (unless on dialysis), platelet count <50,000, WBC >15,000, INR >I.5 (irreversible) or heparin-associated thrombocytopenia.
17. Known cardiac sources of emboli not under treatment with anticoagulant therapy.
18. Atherosclerotic disease involving adjoining vessels precluding safe placement of the guiding catheter or sheath.
19. Planned treatment of non-target lesion within 30 days.
20. Other abnormal angiographic findings that indicate the patient is at risk of a stroke due to a problem other that the target lesion, such as: ipsilateral arterial stenosis greater in severity than the target lesion, cerebral aneurysm, or arteriovenous malformation (AVM) of the cerebral vasculature.
21. Dementia or confusion.
22. The patient is enrolled in another study protocol.
23. Patient may not participate in another investigational trial up to 12 months post-index procedure.

Study Population

The first patient was enrolled on February 20, 2002. Enrollment was completed on March 10, 2004. A total of 488 patients enrolled in the CABERNET trial at 21 participating centers worldwide and 41 of the 488 patients also underwent a contralateral procedure (>30 days following initial index procedure). Thirty-four of the 488 patients were enrolled with "Roll-In" status at 16 centers, yielding a total of 454 (488-34) patients enrolled in the main registry of the trial. Eleven patients did not receive a NexStent at the time of implant and were terminated from the study per protocol, yielding a total of 443 evaluable patients at the time of discharge. Three patients were lost to follow-up (LTF) and 2 patients expired after hospital discharge, with 438 patients available for their 1-month follow-up. There were 2 missed visits yielding 436 patients that completed a 1-month follow-up visit. There were 17 patients that were LTF and 17 patients that expired between the 30-day and 1 year follow-up visits, with 404 patients that were available for their 1-year follow-up. There were 6 missed visits at 1 year yielding 398 patients whom completed their 1-year follow-up.

The data analyses for the purpose of the primary endpoints included follow-up through one year as pre-specified in the study. A summary of patient enrollment and disposition is provided in Table 6.

TABLE 6. Patient Enrollment and Disposition

Patient Population	Index Procedure	30-Days	1-Year
Total Number of Patients Enrolled	488		
Roll-In Patients	34		
Patients Enrolled in Main Trial Registry	454		
Patients Without a NexStent Implanted	11		
Evaluable Patients[1]	443	443	443
Patients Lost to Follow-Up or Withdrawals (Cumulative)	0	3	20
Deaths (Cumulative)	0	2	19
Evaluable Patients Available for Follow-up	443	438	404
Total number of planned visits among evaluable patients			
Total Missed Visits among evaluable patients		2	6
Total Patients Evaluated		436	398
Clinical Assessments Performed		428 (97.7%)	377 (93.3%)
Neurologic Assessments Performed		412 (94.1%)	365 (90.3%)
12 Lead ECGs (30-Day FU Only) Performed		335 (76.5%)	
Duplex Ultrasound Exams Performed		387 (88.3%)	331 (81.9%)
Stroke Scales Performed		412 (93.6%)	354 (87.6%)
Total Patient Follow-up Rate		436 (99.5%)	398 (98.5%)

[1] Evaluable patients only include those that have a NexStent implant.

The majority of the patients enrolled in the trial were asymptomatic, Caucasian males with an average age of 72.5 years. Of the 454 patients enrolled in the main registry 63.7% had an anatomical high risk factor, 19.6% had a comorbid high risk factor and 16.7% had both. In terms of baseline lesion characteristics, the majority of the patients had a de novo target lesion located in the internal carotid artery. The mean baseline lesion stenosis was 71.9% with an average length of 13.9mm and average diameter of 1.3mm. Baseline demographics and lesion characteristics for the patient population are provided in Tables 7, 8, and 9. Baseline lesion characteristics were analyzed by a centralized angiographic core laboratory.

TABLE 7. Baseline Demographics

Patient Characteristic		Patients (N = 454)	% (except as noted)
Age (years)	Mean ± SD		72.5 ± 8.6 yrs
	Minimum to Maximum		46 to 94 yrs
Age by Decade of Life	40-49	6	1.3
	50-59	29	6.4
	60-69	124	27.3
	70-79	194	42.7
	80-89	97	21.4
	>90	4	0.9
Gender	Male	297	65.4
	Female	157	34.6
Ethnicity	Caucasian	414	91.2
	African American	21	4.6
	Hispanic	10	2.2
	Asian	5	1.1
	Other	4	0.9
Patient Classification	Symptomatic	110	24.2
	Asymptomatic	344	75.8
Medical History	Diabetes Mellitus	150	33.0
	Liver Failure	0	0.0
	Dyslipidemia	315	69.4
	GI Bleeding/PUD	29	6.4
	Hypertension	377	83.0
	Uncontrolled Hypertension	6	1.3
	Cigarette Smoker	320	70.5
	Current Cigarette Smoker	83	18.3
	Family Hx Premature ASD	74	16.3
	Significant Aortic Arch Atherosclerosis	5	1.1
	Cardiac Arrhythmia	81	17.8
	Valvular Disease	26	5.7
	CAD	283	62.3
	PVD	178	39.2
	Prior PTCA	119	26.2
	Prior Valve Replacement	21	4.6
	Prior CABG	161	35.5
	Prior Carotid PTA	13	2.9
	Prior Carotid Stenting	12	2.6
	Hx of TIA	124	27.3
	Hx of Stroke	96	21.1
	Family Hx of Stroke	52	11.5
	Hx of Seizures	11	2.4
	Hx of Other Neuro	30	6.6
	Prior Vertebrobasilar Intervention	1	0.2
	Other	73	16.1

TABLE 8. Patient High-Risk Inclusion Criteria

Inclusion Criteria	Patients (N=454)	%
High Risk Category		
Anatomical Only	289	63.7
Comorbid Only	89	19.6
Both Anatomic and Comorbid	76	16.7
Class I - Comorbid	139	30.6
Class II - Comorbid	53	11.7
Anatomical High Risk Inclusion Criteria (A)		
Previous CEA	95	20.9
Total Occlusion of Contralateral Carotid Artery	85	18.7
Previous Radial Neck Dissection or Radiation Therapy to Neck Region	30	6.6
Target Lesion at or above C2 or below Clavicle	25	5.5
Spinal Immobility of Neck (cervical arthritis or other)	54	11.9
Tracheostomy or tracheal stoma	3	0.7
Presence of laryngeal nerve palsy	8	1.8
Bilateral Carotid Artery Stenosis	143	31.5
Class I: Comorbid High Risk Inclusion Criteria (CI)		
Unstable Angina	26	5.7
Severe LV Dysfunction	42	9.3
CHF (NYHA Class III/IV)	40	8.8
Renal Failure (Dialysis Dependent)	5	1.1
Severe COPD	38	8.4
Requires Staged CABG or Valve Surgery	21	4.6
Class II: Comorbid High Risk Inclusion Criteria (CII)		
Patient is ≥75 years of Age	199	43.8
MI within 6 weeks	5	1.1
Requires Staged Peripheral Vascular Surgery	34	7.5
Major CAD (≥70 Stenosis that have not or cannot be revascularized)	64	14.1

Table 9. Baseline Lesion Characteristics (Pre-Procedure)

Angiographic Data (Core Laboratory Assessment)		Results	
Parameter		**Patients (N=454)**	**%**
Lesion Type			
de novo		360	79.3
Restenotic		94	20.7
Lesion Morphology[1]			
Eccentric		327	72.0
Ulceration		169	37.2
Calcification		190	41.9
Target Lesion Length (mm)			
Mean ± SD	n=441[2]	13.9 ± 5.9	
Minimum Lumen Diameter (mm)			
Mean ± SD	n=443[2]	1.3 ± 0.6	
Baseline Percent Diameter Stenosis (%)			
Mean ± SD	n=443[2]	71.9 ± 11.0	

[1] Lesions may have had more than one type of morphology
[2] Lesion length was not available in 13 patients; MLD and Percent Diameter Stenosis were not available in 11 patients.

Trial Results

The primary and secondary endpoints evaluating the safety and efficacy of the NexStent® in the CABERNET trial are presented in Table 10 and 11 respectively. The 30-day primary endpoint MAE rate (all death, stroke and MI within 30 days) was 3.9%. The 1-year endpoint MAE rate for all death, stroke and MI was 11.9%. The rate for the composite 1-year endpoint that includes the 30-day MAEs plus ipsilateral stroke or death from ipsilateral stroke within 31-365 days was 4.7%.

The primary endpoints in this study were further explored through a time-to-event analysis using a Kaplan-Meier (KM) estimator for the survival function. Life table estimates were obtained for:

a. Freedom from major adverse events (All Deaths, Strokes and MIs) at 1-Year
b. Freedom from major adverse events (All Deaths, Strokes and MIs) at 30-Days; plus ipsilateral stroke or death related to ipsilateral stroke at 1-Year.

Angiographic success was defined as less than 50% residual stenosis following completion of the stent implantation and was attained in 97.7% (423/433) of evaluable patients. The mean post-procedure residual stenosis was 20.5% as assessed by the core laboratory and 6.45% as per the visual inspection performed by the treating physician at the completion of the procedure. Acute procedure success, defined as the composite of angiographic success and overall technical success without the occurrence of an MAE within 24 hours, was demonstrated in 395 patients (87.0%).

The primary endpoints of the trial were met. The upper confidence limits for both primary endpoint MAE rates (14.8%, 6.8% respectively) fell below the reference OPC (12.1%) plus an additional delta of 4% established for this study (16.1%), allowing acceptance of

the hypothesis that carotid stenting using the NexStent Carotid Stent and Delivery System with the FilterWire EZ™ Embolic Protection System meets acceptance of the study hypothesis of comparability to CAE in the high-surgical-risk study population.

Table 10. Primary Endpoints (Major Adverse Events)

Major Adverse Events	≤30 days (n=438)		31-365 days (n=421) [1]		Cumulative 0-365 Days (n=421) [1]	
Primary Endpoints	# Patients	%	# Patients	%	# Patients	%
All Death Stroke and MI at 1 Yr.	17	3.9	33	7.8	50	11.9 UCL=14.8%
	# Patients	%Patients (N=438)	# Patients	% Patients (N=404)[2]	# Patients	% Patients (N=404)[2]
All Death Stroke and MI ≤ 30 days; plus the 31-day to12-month event rate defined as any ipsilateral stroke including any death as a result of an ipsilateral stroke	17	3.9	3	0.7	19	4.7 UCL=6.8%
Major Adverse Events by Classification	≤30 days (n = 438)		31-365 days (n = 421) [1]		Cumulative 0-365 Days (n = 421) [1]	
	# Patients	%	# Patients	%	# Patients	%
Death	2	0.5	17	4.0	19	4.5
Stroke	15	3.4	8	1.9	21	5.0
Ipsilateral Stroke	12	2.7	3	0.7	14	3.3
Major	5	1.1	1	0.2	5	1.2
Minor	7	1.6	2	0.5	9	2.1
Non-Ipsilateral Stroke	3	0.7	6	1.4	8	1.9
Major	1	0.2	3	0.7	4	1.0
Minor	2	0.5	3	0.7	4	1.0
Myocardial Infarction (MI)	1	0.2	16	3.8	17	4.0

[1] N=421 for the 31-365 and 0-365 time periods. This includes 398 patients evaluated at 1 year, 19 deaths, and 4 patients that did not have a 1-year visit but experienced an adverse event (398+19+4 = 421).

[2] In an effort to present the most conservative analysis for the MAE rate concerning the composite Primary Endpoint N=404 was used. Seventeen patient deaths that occurred during the 31-365 day time period were not due to ipsilateral stroke and were excluded from this analysis. Therefore N = 404 (421-17=404).

Table 11. Secondary Endpoints

Endpoint	Results		95% Confidence Limit (%)
	n/N	%	
FilterWire Technical Success	454/477	95.2	LCL=93.2
NexStent Technical Success	443/470	94.3	LCL=92.2
Overall System Technical Success	422/454	93.0	LCL=90.7
Angiographic Success	423/433	97.7	LCL=96.1
Procedure Success (Acute)	395/454	87.0	LCL=84.1
Restenosis 50-79%			
(Cumulative 0-6 Month)	55/343[1]	16.0%	UCL=19.7
(Cumulative 0-12 Month)	65/347[2]	18.7%	UCL=22.5
Restenosis >80%			
(Cumulative 0-6-Month)	3/340[3]	0.9	UCL=2.3
(Cumulative 0-12-Month)	9/333[4]	2.7	UCL=4.7
Target Vessel Revascularization (6-Month)	4/443	0.9	UCL=2.1
(1-Year)	9/443	2.0	UCL=3.5

[1] N=343 includes all patients with duplex ultrasound data available at 6 months plus any patient without a 6 month evaluation that had 50-79% restenosis at an earlier evaluation (339+4=343).
[2] N=347 includes all patients with duplex ultrasound data available at 12 months, any patient without a 6 month evaluation that had 50-79% restenosis at an earlier evaluation, (331+16=347).
[3] N=340 includes all patients with duplex ultrasound data available at 6 months plus any patient without a 6 month evaluation that had >80% restenosis at an earlier evaluation (339+1=340).
[4] N=333 includes all patients with duplex ultrasound data available at 12 months, any patient without a 12 month evaluation that had >80% restenosis at an earlier evaluation and 1 patient that had a late 1 year follow-up who had >80% restenosis (331+2=333).

Additional Analysis

The primary endpoints in this study were further explored through a time-to-event analysis using a Kaplan-Meier estimator for the survival function. Life table estimates were obtained for:

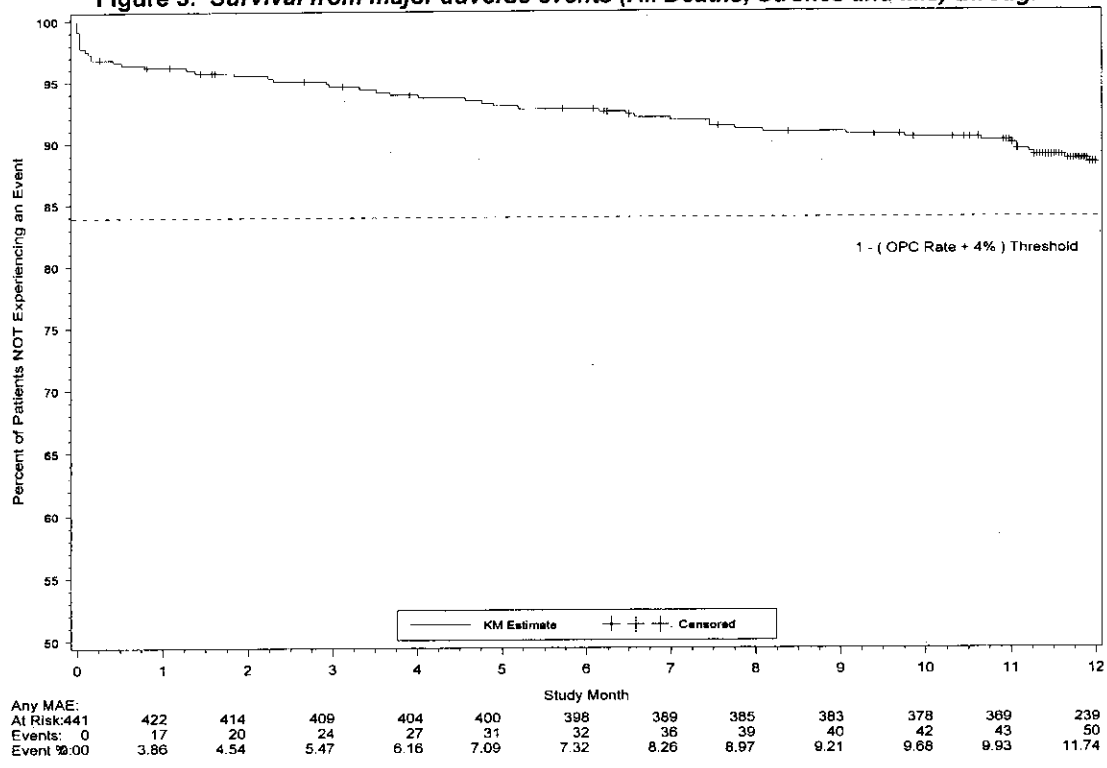
a. Survival from major adverse events (All Deaths, Strokes and MIs) through 1-Year
b. Survival from major adverse events (All Deaths, Strokes and MIs) at 30-Days; plus ipsilateral stroke or death related to ipsilateral stroke through 1-Year.

Endpoint Analysis

Patients were included in these analyses if they had a successful NexStent® implant. The survival time for patients who experienced a major adverse event was calculated as the number of days from the index procedure to the date the adverse event was first identified. For patients who withdrew from the study before the time of analysis, the survival time was calculated as the number of days from the index procedure to the date of their withdrawal. For the composite endpoint, for patients who died of causes unrelated to an ipsilateral stroke, the survival time for the composite endpoint analysis was calculated as the number of days from the index procedure to the date of their death. Patients who were terminated early from the study are considered censored in the analyses performed. Figures 3 and 4 present the KM analysis for each endpoint. Figures 5 through 8 present the KM analysis for asymptomatic and symptomatic patients for each endpoint. The event rate estimate of 11.7% obtained for all death, strokes, and MIs at 12 months from the life table is consistent with the estimate of 11.9% obtained according to the analysis performed per protocol. Similarly, the estimate obtained from

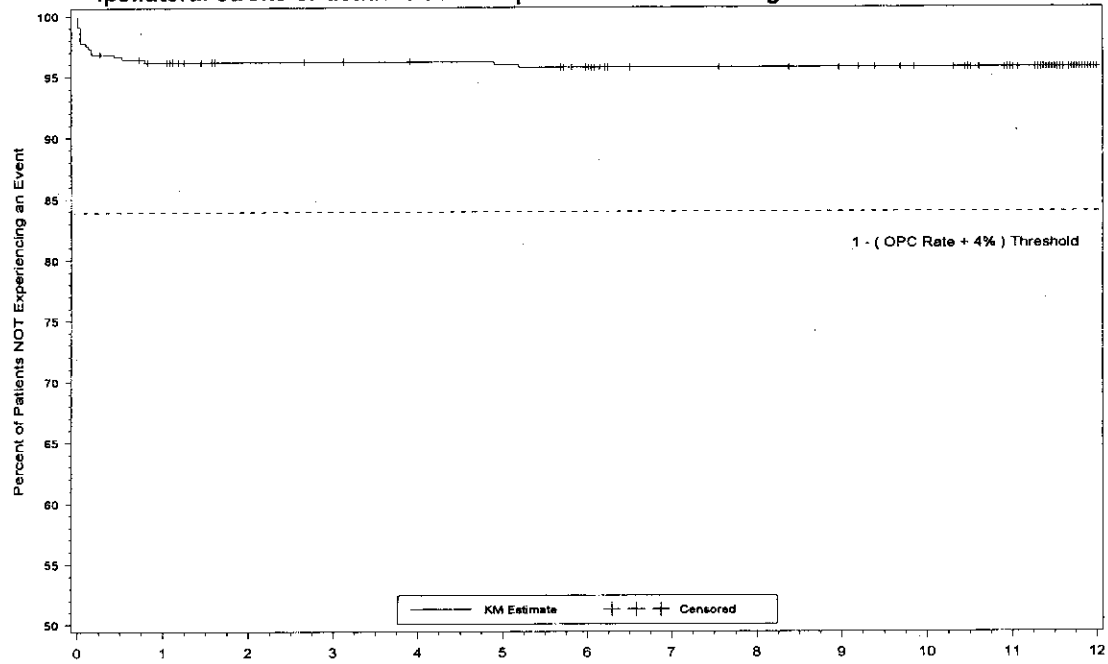
the life table of 4.3% for the event rate for the composite endpoint of major adverse events (All Deaths, Strokes and MIs) at 30-Days; plus ipsilateral stroke or death related to ipsilateral stroke at 1-Year is consistent with the obtained estimate of 4.7% according to the analysis performed per protocol.

Figure 3. ***Survival from major adverse events (All Deaths, Strokes and MIs) through 1-Year***



Any MAE:												
At Risk:	441	422	414	409	404	400	398	389	385	383	378	369	239
Events:	0	17	20	24	27	31	32	36	39	40	42	43	50
Event %	0.00	3.86	4.54	5.47	6.16	7.09	7.32	8.26	8.97	9.21	9.68	9.93	11.74

Figure 4. Survival from major adverse events (All Deaths, Strokes and MIs) at 30-Days; plus ipsilateral stroke or death related to ipsilateral stroke through 1-Year.



Ipsilateral MAE:												
At Risk:	441	421	409	408	406	405	399	390	389	387	383	374	244
Events:	0	17	17	17	17	18	19	19	19	19	19	19	19
Event %	0.00	3.86	3.86	3.86	3.86	4.09	4.33	4.33	4.33	4.33	4.33	4.33	4.33

Figure 5: Survival from Major Adverse Events (All Deaths, Stokes and MIs) at One Year
Symptomatic Patient Group

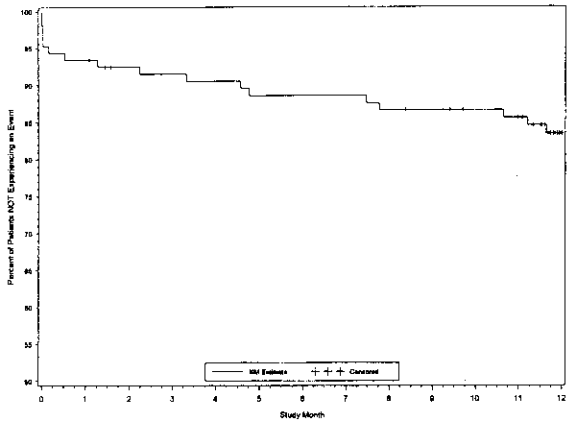


Figure 6: Survival from Major Adverse Events (All Deaths, Stokes and MIs) at One Year
Asymptomatic Patient Group

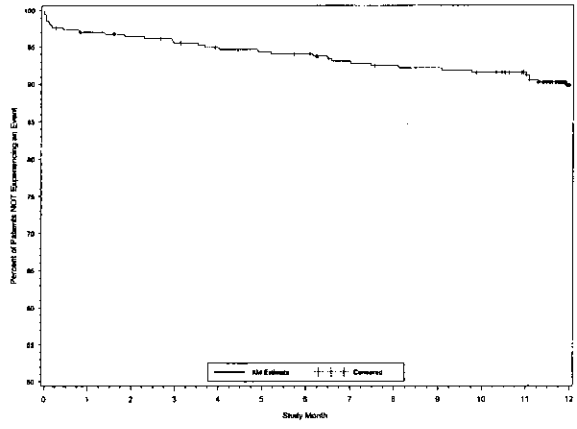


Figure 7: Survival from Major Adverse Events (All Deaths, Stokes and MIs) at 30 Days
Plus Ipsilateral Stroke or Death Related to Ipsilateral Stroke through One Year
Symptomatic Patient Group

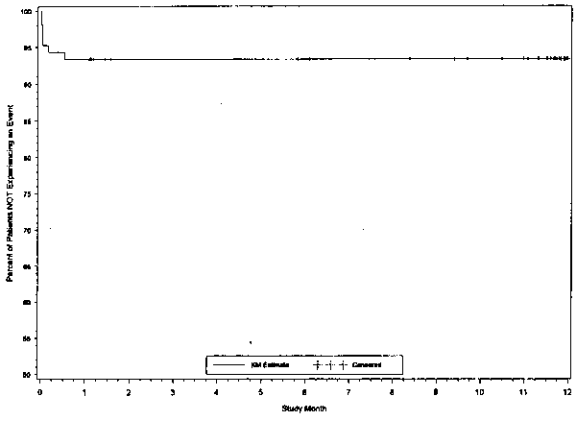
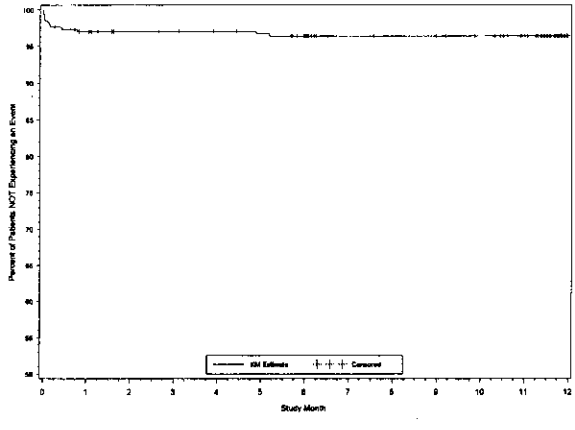


Figure 8: Survival from Major Adverse Events (All Deaths, Stokes and MIs) at 30 Days
Plus Ipsilateral Stroke or Death Related to Ipsilateral Stroke through One Year
Asymptomatic Patient Group



8.0 CLINICIAN USE INFORMATION

WARNING: Do not use after the "Use By" date specified on the package. Assure that the device has been properly stored in a cool, dark, dry place prior to use.

WARNING: The NexStent System is supplied STERILE and intended for single-use only. Do not use if the package is open or damaged. Do not reuse. Do not resterilize as this can compromise device performance and increase the risk of cross-contamination due to inappropriate reprocessing.

Only physicians who have received appropriate training and are familiar with the principles, clinical applications, complications, side effects and hazards commonly associated with carotid stent placement should use this device.

8.1 Materials Required

- 8F guiding catheter or 6F introducer sheath compatible with the vascular anatomy. Minimum guiding catheter / sheath size inner diameter (I.D.) 0.087in / 2.21mm. Guiding catheter or sheath should not exceed 90cm length.
- The NexStent System is not recommended for use with bleedback control hemostatic valves.
- Balloon dilatation catheter (if required)
- FilterWire EZ™ Embolic Protection System with a 0.014in guidewire (190cm)
- 1,000u / 500cc heparinized normal saline (HepNS) (sterile)
- Two to three 5cc syringes

CAUTION: The NexStent System is not compatible with any guidewire larger than 0.014in (0.36mm).

8.2 Periprocedural Care

During the CABERNET clinical study, the recommended pharmacological treatment included aspirin 325mg b.i.d. and either clopidogrel 75 mg b.i.d. or ticlopidine 250mg b.i.d. was started 48 hours prior to the procedure. After the procedure, recommended guidelines included ticlopidine 250 mg b.i.d. or clopidogrel 75mg daily for four weeks, and aspirin 325mg daily indefinitely. A minimum of 70 units/kg of IV heparin (or other approved anticoagulant) was recommended following sheath insertion to achieve a target ACT of ≥275 seconds or appropriate ACT level as determined by the treating physician. Medication therapy for periprocedural care is at the discretion of the treating physician.

WARNING: Appropriate antiplatelet and anticoagulation therapy should be administered prior to, during and post-procedure.

8.3 Pre-procedure

Refer to Section 9.2 of these instructions for the suggested pre-procedure pharmacological treatment regimen. The placement of the stent in a stenotic or obstructed carotid artery should be done in an angiography procedure room. Angiography should be performed to map out the extent of the lesion(s) and the collateral flow. If thrombus is present, do not proceed with stent deployment. Access vessels must be sufficiently patent or sufficiently recanalized to proceed with further intervention. Patient preparation and sterile precautions should be the same as for any angioplasty procedure.

8.4 Stent Size Determination

The NexStent® System is intended for use in reference vessel segment diameters between 4 and 9mm that are <30mm in length.

WARNING: The NexStent System is contraindicated for use with lesions in the ostium of the common carotid artery.

8.5 Inspection Prior To Use

1. Inspect the temperature indicator on the outer box.

WARNING: Do not use if the temperature indicator has exceeded 60°C or has turned from gray to black.

2. Open the outer box and carefully remove the sterile pouch.
3. Before opening sterile pouch seal, inspect for any visible damage such as holes, tears or openings. Do not use the product if any damage to the pouch is detected.
4. Open the sterile pouch and remove the sealed, sterile tray. Inspect the tray for any signs of visible damage such as holes, tears, and openings. Do not use the product if any damage to the tray is detected.
5. Peel open the sterile tray lid and remove the stent/delivery system from the tray and hoop. Examine the device for damage. If it is suspected that the sterility or integrity of the device has been compromised, the device should not be used.

CAUTION: Carefully inspect the NexStent System to verify that the device has not been damaged in shipment. Do not use damaged equipment.

6. Inspect the stent through the delivery system sheath to verify that it has not been damaged during shipment and that the stent remains between the proximal and distal sheath markers. Ensure that the stent is fully covered by the sheath.

CAUTION: Special care must be taken not to handle or in any way disrupt the stent on the delivery system. This is most important during catheter removal from packaging, mandrel removal, placement over guidewire, and advancement through an RHV and guiding catheter hub.

7. Do not use if any defects are noted.

CAUTION: Do not remove the stent from its delivery system as removal may damage the stent. The stent and the delivery system are intended to perform as a system. If removed, the stent cannot be put back on the delivery system.

8.6 Preparation

8.6.1 Delivery System Preparation

CAUTION: DO NOT remove guidewire stylet at this time.

1. Inspect the system visually to ensure that stent is completely constrained within the delivery system and no damage is observed. Do not use the product if any damage to the system is detected.
2. Prepare a 5cc (ml) syringe with sterile heparinized (3%-5%) saline.
3. Attach the provided stopcock to the Y-connection flush port.
4. Turn the stopcock open to the catheter, and loosen the delivery system RHV. Using the 5cc (ml) syringe, flush the delivery system to purge all the air out of the proximal RHV lumen.
5. Tighten the delivery system RHV and continue to flush until heparinized saline exits from the distal end of the delivery system. Close the stopcock, refill the 5 cc (ml) syringe, and reattach it to the stopcock at the Y-connection flush port.
6. Remove the guidewire lumen stylet from the tracking tip.
7. Reopen the stopcock and pinch the delivery system catheter between the fingers at the proximal guidewire lumen, and continue to flush until heparinized saline exits the lumen of the tracking tip. Close the stopcock and remove syringe.
8. Evaluate the distal end of the system and verify that the stent is contained between the distal and proximal stent location markers. The device is now ready for use.

8.6.2 Embolic Protection System Preparation

The NexStent® Monorail® System is indicated for use in conjunction with a FilterWire EZ™ Embolic Protection System. Please refer to the Instructions for Use included with the embolic protection system for information on device preparation and placement.

WARNING: If a filter-based embolic protection system is used, allow for and maintain adequate distance between the filter and the stent delivery system or deployed stent to avoid potential entanglement.

8.6.3 Lesion Preparation

WARNING: Maintain the patient's ACT at >275 seconds throughout the NexStent Monorail System and embolic protection system usage to prevent thrombus formation on the device.

CAUTION: Venous access should be available during carotid stenting to manage bradycardia and / or hypotension by either pharmaceutical intervention or placement of a temporary pacemaker, if needed.

CAUTION: The NexStent Monorail System must be used with a guiding catheter or introducer sheath to maintain adequate support of the 0.014in guidewire throughout the procedure.

CAUTION: Use with bleedback control hemostatic valves is not recommended.

CAUTION: When catheters are in the body, they should be manipulated only under fluoroscopy. Radiographic equipment that provides high quality images is needed.

WARNING: Maintain continuous flush while removing and reinserting devices on the guidewire. Perform all exchanges slowly to prevent air embolism or trauma to the artery.

1. If needed, pre-dilate the lesion with an appropriate size balloon dilatation catheter to a minimum opening of 4mm.

Note: If no pre-dilatation is performed, there must be a minimum luminal opening of 4mm to enable passage of the stent delivery system.

2. Maintain the guidewire position and withdraw the balloon dilatation catheter.

8.6.4 Delivery Procedure

CAUTION: Always use a guide catheter/sheath with a hemostasis valve for the implant procedure. An 8F guide catheter or 6F sheath with a minimum I.D. of 0.087in (2.21mm) is recommended.

1. Cross the lesion using a 0.014in (0.36mm) guidewire (or compatible wire-based embolic protection device) with a working length appropriate for use with a Monorail® Stent Delivery System.

NOTE: For use of any embolic protection system, refer to the Directions For Use of that device for warnings, indications, contraindications and proper use techniques.

2. Angiographically verify that the 5F (1.66mm) profile delivery system can cross the target lesion.
3. If required, careful pre-dilation of the lesion may be done using standard practice PTCA techniques with standard balloon catheters with a minimum diameter of 4mm.

CAUTION: Physicians should use judgment based on experience in dilating arterial lesions and/or obstructions. Never force inflation of a balloon catheter to a point that risks dissection of the arterial wall.

8.6.5 Stent Deployment

WARNING: Ensure optimal positioning of the stent prior to deployment. Once deployment is initiated, the stent cannot be repositioned or recaptured. Stent retrieval methods (use of additional wires, snares and/or forceps) may result in additional trauma to the carotid vasculature and/or the vascular access site. Complications may include death, stroke, bleeding, hematoma, or pseudoaneurysm.

CAUTION: Do not attempt to pull a partially expanded stent back through the guiding catheter or sheath; dislodgement of the stent from the delivery system may occur.

Note: Refer to Figure 2 device diagram.

1. Confirm that the RHV on the guide catheter/sheath is locked to prevent any accidental movement of the guidewire.
2. While maintaining guidewire position, backload the NexStent Monorail System on to the guidewire by introducing the proximal end of the guidewire into the lumen of the tracking tip.

3. Open the RHV on the guide catheter/sheath. Secure the guidewire and catheter/sheath position using one hand. Use the other hand to advance the delivery system over the guidewire distally within the guide catheter/sheath.
4. Prior to exiting the guide catheter/sheath, open the RHV and ensure that bleedback is observed.
5. Under fluoroscopic guidance advance the delivery system until the target lesion is visualized. Advance the delivery system past the lesion and pull back, using the handle, until the lesion is visualized between the distal and proximal stent location markers and slack is removed from the system.
6. Tighten the RHV on the guide catheter/sheath to obtain hemostasis, yet continue to allow the delivery system to freely move through the valve.
7. While holding the guide catheter/sheath, adjust the position of the delivery system handle to minimize or eliminate any slack and/or curvature between the catheter/sheath RHV and delivery system handle.
8. Maintain the position of the delivery system handle relative to the patient during stent deployment. Confirm that the distal and proximal stent location markers are still properly positioned across the target lesion.

CAUTION: Failure to reduce slack and/or curvature of the delivery system catheter between the guide catheter/sheath and delivery system handle during deployment may adversely affect deployment accuracy.

9. Loosen the delivery system RHV. Under fluoroscopic guidance, slowly rotate the deployment control knob counterclockwise to retract the delivery system, and thus deploy the stent.

CAUTION: If, upon initial sheath retraction, the stent delivery system moves relative to the target lesion, discontinue rotating the control knob and re-position the stent delivery system. Once initial stent deployment is fluoroscopically visible and the stent has made contact with the vessel wall, avoid any additional movement of the delivery system.

10. Continue to slowly rotate the control knob counter-clockwise until the proximal end of the stent is fluoroscopically visualized releasing from the delivery system and expanded to the vessel wall.

NOTE: During stent deployment and retraction of the delivery system the distal stent location marker will move towards the proximal stent location marker, thus providing an indication of stent deployment progress. Complete stent deployment is achieved once the distal stent location marker passes the location of the proximal stent location marker by approximately 5mm.

CAUTION: If a strong resistance is met with the introduction of the delivery system or difficulty in initiating release of the stent, remove the entire system from the patient and introduce a new NexStent Monorail System. Do not use a power injector through the delivery system for angiography.

11. Using fluoroscopic guidance, slowly withdraw the delivery system, and tighten the RHV on the guide catheter/sheath to secure wire position and maintain hemostasis.

NOTE: The tracking tip is radiopaque and can be visualized fluoroscopically during advancement and retraction through the lumen of the deployed stent.

12. Using fluoroscopy, visualize the stent to verify full deployment. If further expansion of the stent is desired at any point along the lesion, post-deployment balloon dilatation (standard PTA technique) can be performed.
13. Select an appropriate size PTA balloon catheter and dilate the lesion with standard PTA technique. The inflation diameter of the PTA balloon used for post-dilatation should approximate the diameter of the reference vessel.

CAUTION: Never dilate the stent using a balloon that is larger in diameter than the pre-measured reference vessel diameter.

8.7 Post-Stent Placement

1. Following stent placement, an angiogram should be performed to confirm vessel patency and percent stenosis remaining in the vessel lumen.

WARNING: The stent may cause a thrombus, distal embolization or may migrate from the site of implant down the arterial lumen. Appropriate sizing of the stent to the vessel is required to reduce the possibility of stent migration. In the event of thrombosis of the expanded stent, thrombolysis and PTA should be attempted.

2. Upon completion of the angiogram, the embolic protection system should be removed according to the instructions for use supplied with the device.
3. Patients should be put on an appropriate anticoagulant / antiplatelet regimen such as that described in Section 8.2.

WARNING: In the event of complications such as infection, pseudoaneurysm, or fistulization, surgical removal of the stent may be required.

WARNING: The long-term performance (>1 year) of the NexStent® Carotid Stent has not been established.

9.0 STORAGE

Contents supplied STERILE using an ethylene oxide gas process. Non-pyrogenic. Contents: One (1) NexStent Carotid Stent and Monorail Delivery System, one (1) stopcock connector.
Storage: Store in a dry, dark, cool place and do not exceed 60°C. If the package is properly stored, it may be used on or before its expiration date as printed on the package. Rotate inventory so that stents are used prior to the expiration date on package label.

10.0 REUSE PRECAUTION STATEMENT

Do not use if sterile barrier is damaged. If damage is found call your Boston Scientific representative. For single use only. Do not reuse, reprocess or resterilize. Reuse, reprocessing or resterilization may compromise the structural integrity of the device and/or lead to device failure which, in turn, may result in patient injury, illness, or death. Reuse, reprocessing or resterilization may also create a risk of contamination of the device, and/or cause patient infection or cross-infection, including, but not limited to, the transmission of infectious disease(s) from one patient to another. Contamination of the device may lead to injury, illness or death of the patient. After use, dispose of product and packaging in accordance with hospital, administrative and/or local government policy.

11.0 WARRANTY

EndoTex Interventional Systems, Inc. (EndoTex) warrants that reasonable care has been used in the design and manufacture of this instrument. **This warranty constitutes the entire warranty and is in lieu of and excludes all other warranties not expressly set forth herein, whether expressed or implied by operation of law or otherwise, including, but not limited to, any implied warranties of merchantability or fitness for a particular purpose.** Handling, storage, cleaning and sterilization of this instrument as well as other factors relating to the patient, diagnosis, treatment, surgical procedures, and other matters beyond EndoTex control directly affect the instrument and the results obtained from its use. The product in question must be used according to the Directions for Use, and EndoTex does not warrant this device for in any manner not specified in the Directions for Use. EndoTex's sole obligation under this warranty shall be the repair or replacement of this instrument should it be shown to be defective and EndoTex shall not be liable for any incidental or consequential loss, damage, or expense directly or indirectly arising from the use of this instrument. Any product deemed defective to the satisfaction of EndoTex must be returned to EndoTex for further inspection for this warranty to be operative. EndoTex neither assumes, nor authorizes any other person to assume for it, any other or additional liability or responsibility in connection with this instrument. This instrument must not be reused, reprocessed or resterilized. **EndoTex assumes no liability whatsoever with respect to instruments reused, reprocessed or resterilized and makes no warranties whatsoever, expressed or implied, including but not limited to merchantability or fitness for a particular purpose with respect to such instrument.** In the event that a claim of defect is asserted, submission of such claim must occur with written documentation describing such alleged defect and said alleged defective product must be returned to EndoTex within ninety (90) days of first observation of the alleged defect in order for consideration of this warranty being granted.

Manufactured by:

EndoTex Interventional Systems, Inc.
10231 Bubb Road
Cupertino, CA 95014 USA

Distributed by:

Boston Scientific Corporation
One Boston Scientific Place
Natick, MA 01760-1537
USA
USA Customer Service 888-272-1001

p/n 109-1193
Rev. Draft 10-25-06

Caution: Federal law (USA) restricts this device to sale by or on the order of a physician.

This product contains no detectable Latex.

For single use only. Do not reuse.